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SUBCORNEAL PUSTULAR DERMATOSIS.

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From time to time patients are shown at dermatological meetings who have unusual chronic blistering eruptions not readily recognized as belonging either to the dermatitis herpetiformis or to the pemphigus group. Discussion on these cases is often long, and the diagnoses offered are tentative, dermatitis herpetiformis and impetigo herpetiformis being the most usual.

One of us (I. B. S.) showed such a case at the International Congress of Physicians in London in 1947 and this was afterwards fully reported by Savage (1951) under the diagnosis of Pustular Herpetiform Parapsoriasis. Since then we have shown three other cases—Wilkinson (1951) cases 4 and 5 below; Sneddon (1955) case 6 below—of a vesicopustular eruption of an unusual pattern. We now wish to report three further cases together with a résumé of those previously published by us. We believe that they are all examples of the same condition and that a review of their clinical features will be of value.

Case Reports.

Case 1.—A housewife aged 51 was first seen in November 1953 when she was being treated with thiouracil for mild thyrotoxicosis. Her family doctor sought assistance in controlling what he described as a widespread impetiginous eruption which had not responded to treatment. Slight irritation was present but there was little inclination to scratch.

On examination at that time, a bullous eruption covered her neck, shoulders, arms and breasts. Many intact bullae $\frac{1}{2}$–1 cm. in diameter were present. New lesions

were filled with clear fluid but at a later stage the fluid became turbid so as to form a flaccid blister with turbid pus in the lower part and clear supernatant fluid in the upper part. Blisters tended to form circinate and gyrate patterns, drying and scaling in the centre and spreading at the periphery (Fig. 1). Individual lesions were indistinguishable from bullous impetigo but the whole eruption had some degree of symmetry affecting such areas as the arms and breasts. At a later stage the blisters ruptured and dried forming either leafy scales or superficial crusts. Healed lesions left pigmented stains.

Apart from slight exophthalmos, no abnormality was found on physical examination.

Past History.—No significant illnesses. Menopause at 50. Cultures from intact blisters were sterile.

Blood count : WBC's 6600 (polys. 59% ; lymphos. 39% ; monos. 1% ; eos. 1%). Thiouracil was stopped without any improvement in the skin eruption, and as the clinical appearances suggested some features of dermatitis herpetiformis sulphapyridine 1 g. *b.d.* was given. Slow but definite impovement followed and two months later only pigmented macules remained.

Sulphapyridine was then stopped and within 7 days new bullae recurred on all the previously affected areas and also on the groins and thighs. A biopsy was performed at this time and the histology showed a subcorneal vesicle containing neutrophil polymorphs and an occasional eosinophil (Fig. 2). The epidermis showed spongiosis and a number of migrating neutrophils were to be seen. There was in the upper corium an inflammatory infiltrate which included many eosinophils ; a patchy perivascular infiltrate was also present. Under the influence of sulphapyridine the eruption again slowly cleared in the course of three months. Occasional new blisters continued to appear however, and in March 1955 diamino-diphenyl-sulphone ("dapsone ") 50 mg. *b.d.* was substituted for sulphapyridine. In two weeks a severe relapse occurred. Sulphapyridine was started again and has been continued since then. In December 1955 a relapse occurred during a period of considerable domestic stress but subsequently cleared almost completely. Treatment with thorium-X on two occasions was ineffective.

Case 2.—A housewife aged 65 had suffered for six years from a recurrent blistering eruption on the abdomen and thighs. Severe outbreaks lasted two to three weeks and then subsided ; she was rarely without a few lesions. Acute outbreaks were ushered in by severe itching. During the previous year, treatment with sulphapyridine had not influenced the eruption. In addition she was subject to occasional attacks of asthma and both her sister and niece suffered from hay fever.

Examination revealed numerous gyrate and annular erythematous and blistering lesions. Where they were subsiding a leafy scale could be seen, and in the centre of other lesions crusts gave an appearance of circinate impetigo. Pigmentation was present on the abdomen and in the lumbar region at the site of healed lesions. No abnormal physical signs were found in other systems.

Investigations.—Histology showed a subcorneal aggregation of polymorphonuclear leucocytes with no evidence of acantholytic change in the underlying epidermal cells.

Blood count : WBC 8000. Differential count—no eosinophilia. Culture from vesicles was sterile and no organims were seen on a Gram-stained film. Treatment with dapsone 50 mg. *b.d.* was followed by rapid resolution of the eruption within seven days. The treatment was stopped after some weeks and no recurrence has occurred up to the present.

Case 3.—A single woman aged 54 developed an irritable eruption on the back and in the axillae in April 1955. During the next two months the eruption became more extensive, involving the groins and the chest. The lesions were annular and semicircular with a raised erythematous and bullous edge, leaving pigmentation on healing.

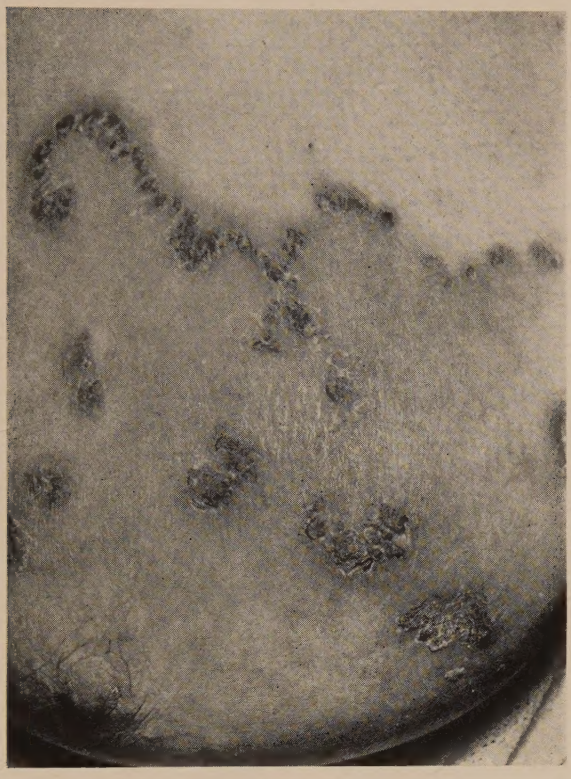

FIG. 1.

FIG. 2.

Histological examination revealed a bulla in the superficial part of the epidermis. At the margin of the bulla, a number of oedema-filled spaces could be seen between the stratum corneum and the stratum granulosum.

The patient was given dapsone 50 mg. *b.d.* and a week later the eruption had almost cleared. The dose was reduced to 50 mg. daily. No skin lesions were present eight months later.

Case 4.—A housewife aged 53 had suffered from mild osteoarthritis for 16 years and developed a recurrent blistering eruption 9 years ago. This first began on the shoulders and by 1946 had become widespread over the whole trunk. After a course of penicillin the eruption subsided but recurred the following spring after the shock

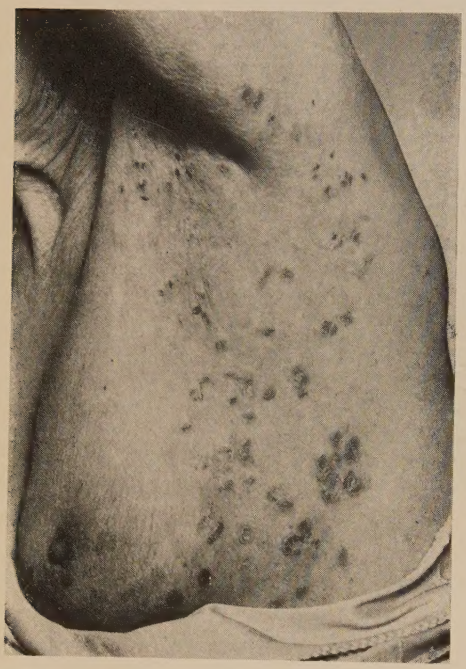

Fig. 3.

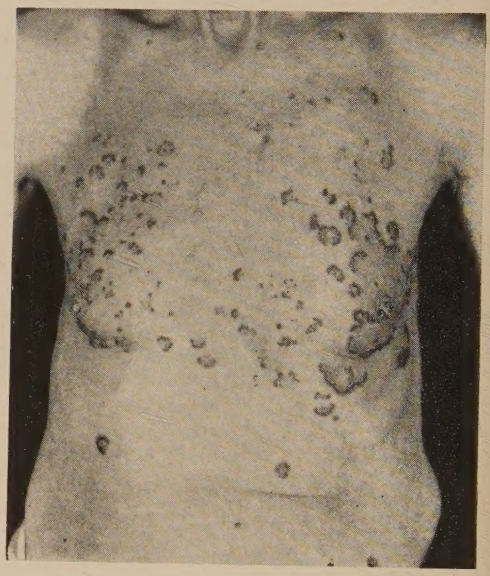

Fig. 4.

of a fall. From that time until 1951 the eruption was constantly present, particularly in the body folds and the proximal parts of the limbs. The hands, feet, face and mucous membranes were never involved and there was no irritation.

The eruption consisted of vesicles rapidly changing to pustules surrounded by a pink areola, the lesion being no more than 1 cm. in diameter. After two to three days the pustules ruptured and dried leaving a brown scab and later an area of discoloration. Numbers of pustules arose in groups and extended centripetally over an area.

Histology of the skin showed subcorneal vesicles containing numerous polymorphonuclear leucocytes. These were also present in the underlying dermis.

Cultures from the vesicles were repeatedly negative. Blood counts and blood chemistry, including the serum calcium, were normal.

Local applications and systemic antibiotics and arsenic had no beneficial effect. Sulphapyridine produced a temporary improvement. Lasting improvement followed local treatment with thorium-X and no relapse has occurred during past three years.

Case 5.—A housewife aged 71 was first seen in 1948, soon after she had developed a pustular eruption on the neck and breasts and in the axillae and groins. The eruption persisted, phases of activity alternating with periods of quiescence. Slight irritation occurred when the patient was warm. The lesions consisted of vesicopustules surrounded by an erythematous areola. During the course of a week the pustules dried, leaving at first a yellowish flake and later a discoloured macule. All the main folds of the trunk and proximal parts of the limbs were affected and the eruption appeared to spread outwards lesion by lesion (Fig. 3).

Histological examination showed subcorneal bullae containing polymorphonuclear leucocytes.

Cultures from pustules grew *Staphylococcus albus*. Blood counts and blood chemistry were normal. No form of treatment, including several applications of thorium-X, controlled the eruption but recently dapsone 50 mg. daily has produced a striking and definite improvement.

Case 6.—A retired clerk, a man of 68, had suffered since 1947 from recurrent attacks of an irritable vesicopustular eruption. The rash started on his chest, extended to the axillae and groins, and has continued to affect all these areas.

Severe outbreaks occurred every three months or so and gradually died away in three to four weeks, though he was seldom completely free from lesions. Since June 1954 the eruption had been more severe than before and itching a more prominent feature. He took no drugs and his general health had been good.

Past History.—Rheumatic fever when aged 21, prostatectomy at age 60.

Examination.—The patient has been under observation since 1947 and during this time the eruption has consisted of vesicopustules which have extended into serpiginous, scaling and crusted lesions with central clearing (Fig. 4). The face and mouth have always been spared, the axillae, groins and chest principally affected. Slight pigmentation was left when the lesions healed.

Histology.—A small subcorneal bulla is present in the epidermis. Numerous polymorphs are present in the blister and extend down a hair follicle in its floor.

Comment.

The main feature of these cases is the onset in middle life of a recurrent vesicopustular eruption which runs a harmless but protracted course over a number of years.

All but one of our patients are women and the average age of onset has been 54·8 years, the youngest being 41 and the oldest 68. The duration of the disease has varied from three months to nine years with an average of 5·8 years. The axillae, groins, abdomen and flexor aspects of the proximal parts of the limbs have been particularly affected. The hands, feet, face and mucous membranes have been entirely spared. The individual lesions consist either of a pustule from the start or of a vesicle which rapidly becomes a pustule, flaccid, turbid and often oval rather than circular ; there is a faint and short-lived erythematous flare surrounding it at the beginning. Within a few days the pustule ruptures, leaving a scale or crust. Pustules tend to collect to form little groups of annular or gyrate shape with an actively spreading edge, incomplete and irregular, in which are seen pustules, crusts and in places leafy dry scales about to fall off. After healing, either a reddish stain or sometimes a more definite brown pigmentation is left. There is no atrophy.

This configuration spreads outwards in an irregular arc from the folds of the breasts, armpits and groins on to the adjoining areas of the body. In successive attacks the same area of skin may be completely involved and further spread may occur at the periphery, or isolated groups of pustules may form within the now pigmented area and die away before they have spread very far. The eruption has phases of alternate quiescence and activity lasting a few weeks though in some cases the skin has been almost continuously affected by successive waves of pustules overlapping each other. On the other hand the eruption may subside completely after an attack and a spontaneous remission occur, lasting several months.

Irritation was a feature of cases 2, 3 and 6 but was absent in the others. Even in those who complained of irritation, excoriation did not occur. The general health of the patients has been unaffected and none have ever suffered from febrile episodes either before or during the eruption of fresh blisters.

No abnormality in blood counts has been found. Blood Wasserman and Kahn tests have been consistently negative and blood chemistry within normal limits. Cultures from intact pustules and vesicles have either been sterile or have grown *Staphylococcus albus* or *Staphylococcus aureus*. *C. albicans* was not found.

The constant histological feature of every case has been a subcorneal blister filled with polymorphonuclear leucocytes. No change in the epidermal cells, such as acantholysis, has been seen and usually oedema was absent in the epidermis, though spongiosis was observed in one case. Polymorphonuclear leucocytes were sometimes also found in the upper corium and here there seems to have been an increase of eosinophils in some cases. Some but by no means all of the blisters have communicated with hair follicles.

Local or systemic treatment with antibiotics has not influenced the eruption. The results obtained with other methods are summarized in Table I.

TABLE I.

	Beneficial effect of:			
	Liq. arsenicalis.	Sulpha-pyridine.	Diamino diphenyl sulphone ("dapsone").	Thorium-X.
Case 1	Not used	Good	None	None
„ 2	None	None	Good	Not used.
„ 3	Not used	Not used	„	„ „
„ 4	None	Poor	Not used	Good.
„ 5	„	„	Fair	Poor.
„ 6	Good	None	Good	Not used.

(Thorium–X was used after Savage (1951) had demonstrated its beneficial effect in his case.)

It will be seen that diamino-diphenyl sulphone (" dapsone ") was successful in 3 and partly successful in another one of the 5 cases in which it was used, and appears therefore to be the most effective remedy.

Discussion.

The work done in recent years on the microsocopical appearance of blisters has enabled us to place most of the bullous eruptions into fairly well defined groups. Thus, in dermatitis herpetiformis and pemphigoid the characteristic findings are vascular dilatation, oedema and a sub-epidermal bulla ; acantholysis is absent. In pemphigus, including the Senear-Usher syndrome, the bulla arises as a result of intra-epidermal cleavage, and it contains acantholytic cells. In benign familial pemphigus, both acantholysis and dyskeratosis occur. The blisters we have described appear histologically to be quite different. Although they are similar to those of impetigo contagiosa, an infective basis for the eruption can be excluded by the clinical features, the very protracted course, and the complete failure to respond to local and general antibiotics.

It is also clear that the eruption we have described is unrelated to impetigo herpetiformis as originally described in pregnant women by Hebra (1872) and by Kaposi (1887). It is true that a number of milder cases, and some occurring in men and children, have been described under the same name since that time, but these probably include a wide variety of heterogeneous cases of varying pathology. Beek (1951) has divided impetigo herpetiformis cases into three groups : (i) Occurring in pregnant women ; (ii) with hypoparathyroidism ; and (iii) in women who are not pregnant and in men.

The third type of case has usually been associated with acute toxic illness and fever, as in the patient described by Fletcher-Hall (1944). That impetigo herpetiformis is indeed a serious condition is indicated by a mortality of over 50% in most recorded series (Le Coulant, 1950). The mucous membranes are often affected and the condition is always accompanied by some degree of disturbance of the general health.

The histological features of impetigo herpetiformis have been described by Lever (1954) as resembling acrodermatitis continua, with acanthosis and a sponge-like network in the stratum malpighii filled with neutrophil polymorphonuclear leucocytes. This differs greatly from the histology of our cases.

The peculiar distribution of the eruption as well as the response to sulphone therapy make it difficult to regard these cases as representing any form of parapsoriasis.

We have found reference to four cases which resemble closely those we have described. The earliest, that of Wende and Pease (1901) was entitled " Atypical Pustular Dermatitis Herpetiformis ". Their patient had a recurrent

superficial pustular eruption, but attacks were at times ushered in by fever and the pustule was situated in the middle of the epidermis—much deeper than was the finding in our cases.

Simpson (1948) demonstrated a 59-year-old farmer who for 4½ years had had an itching pustular eruption on the trunk and proximal parts of the limbs. The eruption waxed and waned and occasionally complete remissions lasted several weeks. Histology of the eruption showed a subcorneal pustule. Treatment with sulphapyridine and arsenic was ineffective. This case sounds to be identical with ours and Simpson, who saw our Cases 4 and 5, believed them to be of the same nature.

Carney (1952) reported another example under the title of " Dermatitis Herpetiformis, ? Impetigo Herpetiformis, ? Monilia " and in the ensuing discussion, dermatitis herpetiformis and impetigo herpetiformis were the suggested diagnoses.

Cipollaro (1954) described a recurrent subcorneal pustular eruption in a man of 51. This failed to clear on sulphapyridine and the tentative diagnoses were dermatitis herpetiformis and pemphigus. We also have personal knowledge of two other unpublished cases—Meara (1956) and McGibbon (1956)—which have cleared on dapsone.

Enough has been said about the features of these cases to distinguish them from erythema gyratum perstans and any variety of the annular erythemas.

Although in its protracted course and its response to dapsone the condition bears some resemblance to dermatitis herpetiformis, there are many features which do not conform to the usual clinical picture of that disease. Itching is not a feature of most of the cases ; the distribution is predominantly flexural, involving mainly the axillae and groins ; in two cases there was a favourable response to applications of thorium-X. Most important of all, the histology of this characteristic subcorneal pustule has not been described in dermatitis herpetiformis. The features of dermatitis herpetiformis, impetigo herpetiformis and the present disorder are contrasted in Table II.

It should be mentioned that Duhring was well aware of a pustular form of the disease bearing his name and described, in 1887, a case of " Dermatitis Herpetiformis of the Pustular Variety ". The account he gives of this and other cases suggests that there may be some relationship between them and the cases we have described, but there are many respects in which they are not similar. The course of this pustular form of dermatitis herpetiformis appears to be variable but to be associated, at any rate during some of the time, with extreme itching. Although Duhring comments on a phase of disseminated small pustules, the lesions were at other times " seated upon an angry looking, drawn-up, puckered base ". The eruption was present on the trunk, shoulders and buttocks and the variation in the severity of the course distinguished it from our cases with a predominantly flexural distribution and almost symptom-

TABLE II.—*Diagnostic Features.*

	Dermatitis herpetiformis.	Impetigo herpetiformis.	Subcorneal pustular dermatosis.
Sex and age	More males, all ages	(*a*) Pregnant females; (*b*) Older females; (*c*) Men and children (rare)	More females, 40–70.
Distribution	Extensor points	Flexures, trunk and limbs	Flexures, trunk and proximal limbs.
Mucosal lesions	Sometimes	Frequently	Never.
Itching	Severe	Absent	Variable or absent.
Pigmentation	Usually marked	Absent	Moderate or absent.
Course	Prolonged, with remissions	Hectic, febrile	Prolonged, with remissions.
Mortality	None	High	None.
Blood findings	May be eosinophilia	May be hypocalcaemia	Normal.
Other diseases	None	Hypoparathyroidism; Pregnancy; ? Hormonal upset	None.
Histology—Pustule	Subepidermal	Intra-epidermal	Subcorneal.
Dermis	Oedema, vascular dilation	Marked inflammatory infiltrate	No marked changes.
Variation in pathological changes	Wide	Narrow	None.

less course. There is no mention of the histology in his report. The consistent finding in our cases of pustules in the subcorneal position provides a distinctive feature which separates this condition from the others we have mentioned. We therefore prefer to regard these cases, provisionally at least, as representing a separate entity.

SUMMARY.

Six cases of a chronic vesicopustular eruption, which affects mainly middle-aged women, are described.

The pustular nature of the eruption, which histologically shows a subcorneal blister filled with polymorphonuclear leucocytes, has been a feature of all the cases. Diamino-diphenyl-sulphone (dapsone) was successful in controlling the eruption in 4 of the 6 cases. It is suggested that the eruption is distinct from dermatitis herpetiformis though similar in the grouping of its lesions, its protracted course and its response to remedies.

Until its position as a separate entity or otherwise has been established, we suggest the descriptive name of " subcorneal pustular dermatosis ".

Postscript.—More recently, a seventh case—a woman of eighty—has been under the care of I.B.S. Her eruption was identical with the above cases though it involved the whole trunk and proximal parts of the limbs. Cultures from the pustules were sterile and a specific search for *Candida albicans* was negative. Applications of nystatin ointment were without benefit.

Case 5 has also been investigated afresh in 1956. No evidence of *Candida albicans* infection was found and nystatin orally and locally was of no benefit.

We are confident that the dermatosis is not a fungus infection.

We are most grateful to Dr. Ian Anderson for allowing us to study Case 2 ; to Dr. Peter Borrie for the clinical details and sections of Case 3, and to Dr. G. B. Dowling for his help and advice.

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GENERALIZED PUSTULAR BACTERID. ITS RELATIONSHIP TO THE PUSTULAR DERMATOSIS OF SNEDDON AND WILKINSON.

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In 1947 Sneddon showed a patient at the International Conference of Physicians who suffered from a recurrent vesiculo-pustular eruption on the chest and subsequently in the axillae and groins; histologically the lesions showed vesicles containing polymorphs and lying just below the horny layer. The patient was later presented at the Royal Society of Medicine (Sneddon, 1955) where two similar cases had previously been shown by Wilkinson (1951). Although the eruption in some respects resembled dermatitis herpetiformis—indeed Sneddon labelled his patient "dermatitis herpetiformis (erythemato-squamous type)"—both authors thought their cases showed distinct differences from the classical picture and that their condition was a specific entity. Some doubt was cast on this at the joint meeting of the British and French dermatologists in July, 1956; but those who saw the original cases at the Royal Society of Medicine, including the writer, agreed that they showed a specific condition whose relation to other skin diseases was as yet uncertain. The patient about to be described does, I believe, throw considerable light on the nature of the eruption and indicates that it is related to the recurrent pustular lesions of the palms and soles which were called by Andrews "pustular bacterids".

Case Report.

A man aged 54, an excavator driver.

History.—In June 1946, when aged 44, he developed small pustules on the left palm and in August these appeared under both insteps. He was seen in March 1947 and treated with sulphathiazole, Whitfield's ointment and later three doses of 150r x-rays without much benefit. In March 1952 he started to develop blistered lesions on his trunk in addition to the pustular lesions on the palms and soles which have never cleared.

On 9 : vi : 52 he was admitted to hospital for complete investigation. His general health was only fair as he complained of rheumatism in his knees and said he tended to be chesty in winter. He showed typical intra-epidermal pustules of the "pustular bacterid" type (Fig. 1) on the palms and soles. On the trunk, especially on the sides, were circinate and guttate scaling erythematous patches showing evidence of preceding vesicobullous formation of which traces remained around the edges. These lesions varied in size up to about an inch in diameter and were obviously developed from small pustules, several of which were scattered about unruptured (Figs. 2, 3). The lesions were also present on the limbs, especially over the elbows, but were not psoriasiform. The genitals and mucous membranes were not affected.

General physical examination was normal except for a raised blood pressure—200/120. There was no evidence of oral or nasal sepsis.

Investigations.—Blood count: Hb: 106%. RBC: 5,100,000. WBC: 8700. Normal differential. ESR: 45 mm. 1 hr. Serum proteins 7·2%; Alb. 3·9%: Glob. 3·3%.

Swab from pustules—sterile. W.R. negative.

Urine after prostatic massage—normal.

Patch test to 5% potassium iodide—negative. No exacerbation followed the ingestion of iodide.

FIG. 1.

FIG. 2.

X-ray of abdomen normal, with normal renal outlines.

X-ray of chest and tomography showed three rounded opacities in the lung fields. The patient was seen by Mr. Allison, the chest surgeon, who at that time thought the opacities might be metastatic abscesses. The patient has been x-rayed periodically ever since and there has been remarkably little change in the lungs over 4 years. The nature of these lesions is still uncertain but in 1954 Mr. Allison thought they might possibly be tuberculous. The patient has remained in good health ever since.

Histology.—Biopsies were taken on two occasions from the trunk and both showed vesicular spaces filled with polymorphs lying just under the horny layer. The earliest lesion is a tiny vesicle splitting the horny layer from the granular layer, the remains of which forms the floor of the blister. There is no acantholysis but there is some spongiosis of the prickle cells immediately under the lesion; the deeper layers are normal. The vesicle contains polymorphs and some round cells with a little keratinous debris.

The dermis is normal except for a little perivascular round-cell infiltration.

In more advanced lesions the blisters are larger but still subcorneal in site. They contain many polymorphs and some round cells, and here and there a few degenerating prickle cells which have been split off the floor. There is more marked perivascular infiltration with round cells and histiocytes in the dermis.

Course.—There was no response to Aureomycin, 250 mg. *q.i.d.*, but the skin lesions cleared rapidly on sulphapyridine, ½ g. *t.d.s.* and he was discharged from hospital on

Fig. 3.

3 July. On 15 August he reported that every time he took sulphapyridine it upset him and his eyes became bloodshot, so the drug was stopped. From then the skin lesions waxed and waned, but never cleared despite treatment with liq. arsenicalis, antrypol, vitamin D_2 (600,000 units weekly), antihistamines, and isoniazid, the latter given in view of his lung x-ray picture. His general condition was satisfactory apart from some osteo-arthritis in his knees.

From 15 : x : 54 he was given diaminodiphenylsulphone 25 mg. b.d., and within 8 days his skin including the palms and soles had cleared. On 10 : xii : 54 there were only stains on the trunk and minimal lesions on the hands, and the dose was reduced to once a day. From then on he started leaving the dapsone off periodically; at first he relapsed after 3 days without dapsone but by October he managed 3 weeks and from March to July 1956 he only had to take about 10 doses, any relapse being controlled within about 4 days.

To summarize, this man developed a typical "pustular bacterid" on the palms and soles in 1946, and in 1952 subcorneal pustules on the trunk which evolved into scaling circinate lesions. The pustules were sterile. The rash improved with sulphapyridine but he could not tolerate this and it had to be

stopped. From then the rash resisted all treatment till October, 1954, when he was given dapsone which controlled the eruption at once. The skin has remained practically clear since, any relapse being quickly suppressed by a few days' treatment.

The resemblance of the lesions on this patient's trunk to those described by Sneddon and by Wilkinson is striking. The former states " the skin eruption . . . consists of a primary vesico-pustule which extends into a serpiginous scaling and crusted lesion with central clearing " ; this could equally refer to my case. The distribution in all was mostly on the trunk and upper arms though in my case the axillae and groins were not especially involved as seems to have been the tendency in the other cases. In none of the patients, including mine, was the mouth affected. The histology in all the cases was identical. The course of my case and Sneddon's was exactly similar with failure to respond permanently to any treatment until dapsone was tried when the blisters cleared rapidly. It may be a coincidence that both patients were intolerant of sulphapyridine.

From the above evidence I have little doubt that the condition shown by my patient on the trunk is the same as that in these two authors' patients. It seems also reasonable to assume that the pustular eruption which my patient developed on his trunk in 1952 was the same as he had on his hands from 1946, since in both the pustules were intra-epidermal, waxed and waned together, and responded to the same treatment after resisting other forms of therapy. The lesions on the hands and soles persisted for 6 years before there was any eruption elsewhere and were typical of a " pustular bacterid". I therefore believe that the lesions described by Sneddon and Wilkinson are the same disorder but appearing in an uncommon site and therefore assuming a somewhat different appearance.

One cannot discuss fully here the nature of the so-called " pustular bacterid". Andrews believes that it is caused by toxins from a septic focus, especially in the throat or mouth, and claims that the rash disappears on removal of such a focus. Although I have seen occasional dramatic improvement following tonsillectomy or the removal of an infected tooth, the majority of patients do not respond and even those who do, almost always relapse (Everall, 1956). This suggests that any influence sepsis may have is in the nature of a trigger on a pattern reaction and not the fundamental cause. The association of intra-epidermal pustules with psoriasis of the palms and soles is so frequent that some authors have thought that " pustular bacterids " are really a form of psoriasis and that the intra-epidermal pustules are an exaggeration of the Munro-Sabouraud abscess of psoriasis. In many cases this may indeed be true or it may be that the " pustular bacterid " picture is superimposed on psoriasis but there are many cases, like my patient, in which all evidence of psoriasis is lacking and we are dealing only with a pustular eruption. In the earliest

lesion examined histologically in my case there is no suggestion of psoriasis—no clubbed papillae, no dilated papillary vessels and no parakeratosis. I believe therefore that this syndrome of intra-epidermal pustules can occur alone, though it may also, not infrequently, be associated with psoriasis.

The response of both my case and Sneddon's to dapsone is remarkable and suggests at first sight that the condition might be related to dermatitis herpetiformis. This is really unlikely in view of the entirely different histological picture and, in my patient, the lack of any flare-up with potassium iodide both applied locally and given internally. The mechanism of the response of dermatitis herpetiformis to dapsone and to sulphapyridine is quite unknown. There have been reports of cases of " pustular bacterid " controlled by sulphapyridine but I know of no record of the action of dapsone in this condition ; we are at the present time investigating this subject. Should it be shown that " pustular bacterid " does improve with dapsone this would be further evidence that the condition of chronic recurrent subcorneal pustules is a form of pustular bacterid.

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HIDROACANTHOMA SIMPLEX.

An Assessment of a Selected Group of Intraepidermal Basal Cell Epitheliomata and of Their Malignant Homologues.

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Jadassohn (1926) drew attention to the intraepidermal development of basaliomata wherein one finds sharply demarcated areas of small cells with dark nuclei in the rete. Jadassohn was convinced of a multicentric origin. He had not found any similar cases in the literature apart from an annotation by Borst (1904) who postulated an intraepidermal spread for his " extraordinary cancer of the lip ". This tumour showed a basocellular structure, but of the type one associates with ordinary rodent ulcers—irregular and thickly heaped cells gradually coming to involve large sections of the epidermis together with marked palisading of the basal layer. These features of the initial lesion make it unjustifiable to apply a " Borst-Jadassohn " label to the nest-like basaliomata with small uniform cells as has been done by some authors. Histological accounts of such neoplasms are now included in some recent textbooks (Ormsby and Montgomery, 1954 ; Eller and Eller, 1952 ; Lever, 1954).

Since Jadassohn's description these tumours have generally been accepted as basal-celled but Montgomery (1929), quoting one case, described the rete ridges as containing both squamous and basal growths. Haber (1954) regards the unit of this " peculiar type of intraepidermal epithelioma " as a prickle cell : his Fig. 7 shows a nest of completely keratinized cells with glossy eosinophilic cytoplasm. Haber points out that sometimes the neoplastic squamous cells contain melanin and there may be associated dendritic cells ; but this, he suggests, should not make one think of intraepidermal naevi as the melanoblasts appear normal. We think that too much attention has been given to the individual cell as a means of classification ; the structure of these tumours is only understandable in terms of their behaviour en masse.

The histological picture of the Jadassohn type of intraepidermal basalioma is so striking as immediately to suggest a specific type of lesion. After a careful survey of the many varied patterns of superficial skin tumours we have become

convinced of the *sudoriferous* nature of these multifocal epitheliomata. Judged teleologically, the typical Jadassohn lesion may be regarded as the formation of multiple " sweat germs " within the substance of the epidermis. The chief evidence for this contention is :

(i) The occurrence of undoubted sweat glandular differentiation in a proportion of cases.

(ii) The primary origin of strictly similar neoplasia in the sweat appendages themselves.

(iii) An occasional co-existence with subepidermal sweat-gland tumours.

Apart from the usual lack of obvious sudoriferous differentiation, two reasons may be advanced for the non-recognition of this epidermal adaptation.

(i) The failure of histologists to identify the classical Jadassohn with other kindred lesions in which the nest-like arrangement is less pronounced but which may show tubular differentiation—sometimes of such degree as to mimic pre-existing sweat apparatus.

(ii) The inadequacy of conventional methods of classification, which do not recognize that neoplastic rete cells may be of an adnexal instead of an epidermal type.

The ensuing account covers the histological range of the tumours to which we apply the name of " hidroacanthoma simplex ". We employ " acanthoma " as a general term for benign or malignant neoplasms arising mainly in the rete ; their derivation from an epithelium normally composed of prickle cells justifies this name. " Simplex " refers to the limitation of the potential or actual differentiation to a pure sweat glandular type. For descriptive purposes the neoplastic cells may be regarded as forming cellular *matrices* within the epidermis.

Tumours of the apocrine gland-bearing areas (axillary, areolar, ano-genital, eyelash, external meatal) do not fall within the scope of this paper.

Benign Hidroacanthoma Simplex.

In this category are included many lesions of the Jadassohn type together with some close relatives in which the multifocal structure is much less emphasized. Any of these patterns of neoplasia is extremely rare.

The matrix cells.—The majority of the matrix cells are of an immature type with dark hyperchromatic nuclei resembling normal epidermal cells of the deeper rete. The striking feature is the uniformity in size and spacing of the new cells and of their nuclei as they lie in the rete. Each cell possesses a rim of cytoplasm of a finely striated appearance which tends to be a little less eosinophilic than in normal epidermal cells ; the nucleus is sometimes separated from the cytoplasm by a perinuclear halo or space. The cell borders have sharp

contours and the intercellular bridges are well preserved. Foci of tightly packed parakeratotic cells lie superficial to many of the matrix cell groups and may on occasion extend down into them as a central plug.

These small parakeratotic cells are produced by the maturation of the deeper and less mature matrix cells. Considerable variation in this style of maturation is to be seen. Small numbers of cells become keratinized in globular form leading to eosinophilic elements like the *grains* of Darier. Rarely accumulations of hyalinized cells are found in the centres of groups of matrix cells ;

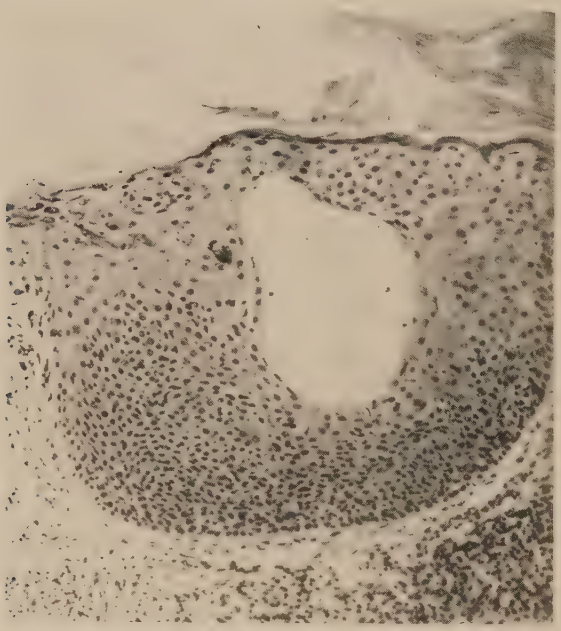

FIG. 1.—Circumscribed necrotic area in rete produced by cell necrosis. Tumour of upper chest. × 140.

similar cells may be numerous in tumours of the sweat glands and it is doubtful whether such elements should be regarded as true examples of individual cell keratinization. An alternative form of maturation which contrasts with the foregoing is associated with a partial disappearance of the eosinophilic components of the cytoplasm ; in this way are created masses of paler, somewhat larger cells with prominent heavily contoured borders between which the intercellular bridges are for the most part well preserved. Another common and closely allied feature is the disintegration of whole groups of cells, a process attended by the formation of a basophilic substance, which is seen as circumscribed lakes lying in the rete (Fig. 1).

Organization.—These neoplasms usually form plaques, as a rule but little raised above the surface of the skin, and may be either verrucose or plane.

In the verrucose forms the line of junction of the stratum corneum and the cellular rete is markedly sinuous, though the tumours still tend to preserve an overall flatness (Fig. 2). There is a generalized hyperkeratosis in addition

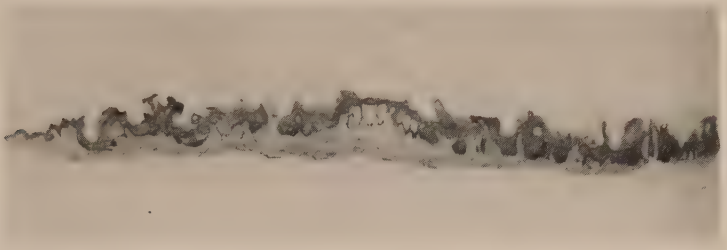

Fig. 2.—Hidroacanthoma simplex. Verrucose form. × 6½.

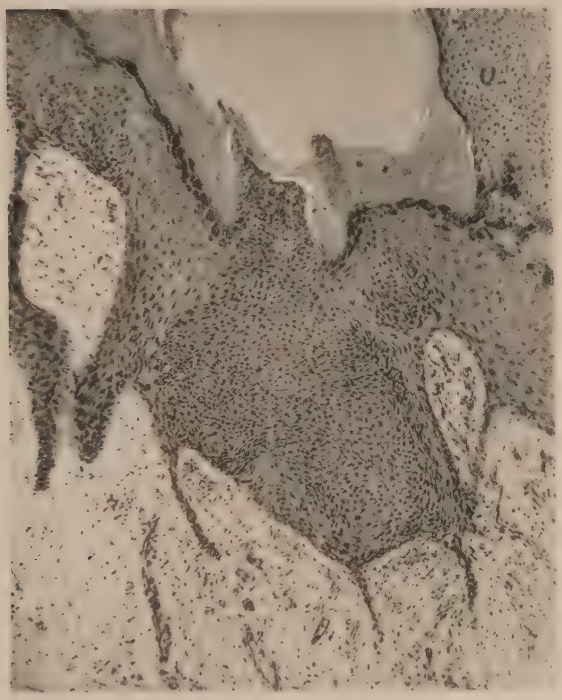

Fig. 3.—Same tumour as in Fig. 2. Circumscribed nests of matrix cells in rete. × 107.

to the focal parakeratosis. The verrucosity is due to a non-specific overgrowth of the epidermis and the tumour matrices lie in an acanthotic rete as discrete and circumscribed nests of cells; the distinction between the latter and the surrounding epidermal cells is obvious (Fig. 3). The immature matrix cells are mostly of a small basal type; the usually angulated nuclei are invested by a narrow rim of cytoplasm. There may be some whorling among the cells.

From the under-surface of the rete thin epithelial strands reminiscent of sweat ducts run down into the papillary layer of the dermis.

In the plane varieties the surface is much flatter (Fig. 4). The parakeratosis may be focal or widespread ; if the former it may present clinically as small

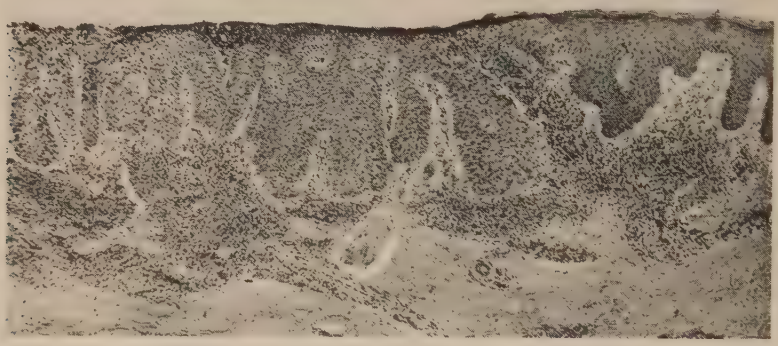

FIG. 4.—Plane variety of hidroacanthoma simplex from left thigh. Widespread compact parakeratotic scale. × 60.

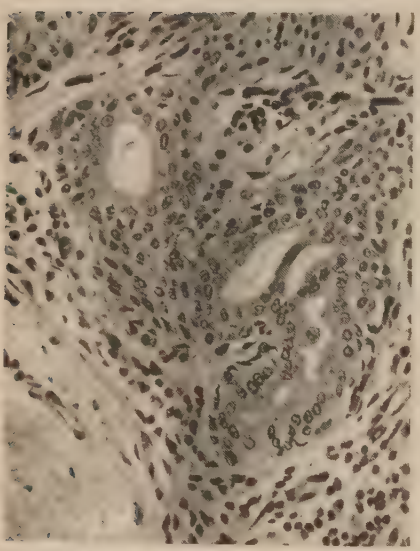

FIG. 5.—Newly formed duct in rete peg. Ghost cells in lumen. × 275.

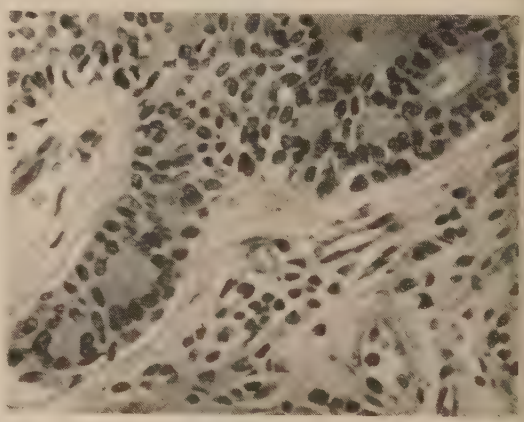

FIG. 6.—Fine tubular differentiation of acinar and duct type. × 425.

discrete plugs peppering the surface. The rete ridges are broadened and the papillae relatively narrowed, favouring the arrangement sometimes referred to as "fused rete pegs" (Haber, 1954). A large portion of the original epithelium is replaced by the new matrices which are introduced into the rete partly as nests and partly in a diffuse manner. The immature matrix cells are

in general plumper than in the verrucose forms and have round or spindle nuclei.

Such evidence as we possess suggests that the plane tumours have a greater capacity for differentiation, especially if downward growth is at all marked. The neoplasm, part of which is depicted in Fig 5, came from the thigh of a woman of 53 years, the only other lesion being on the calf. In many places downward growth of the rete has occurred, mostly in the form of broad masses of epithelium but with some narrow finger-like projections. In these down-growths and in the deeper rete itself unmistakable and clear-cut sweat-glandular

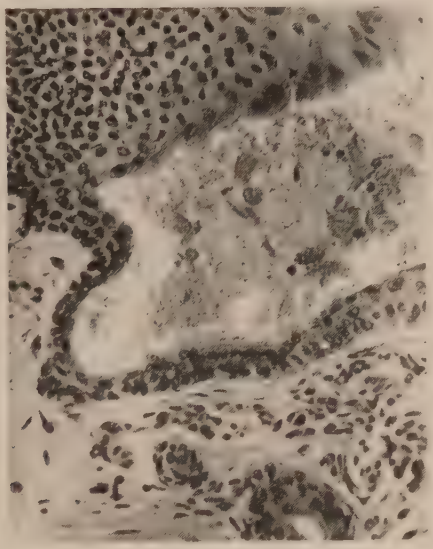

FIG. 7.—Coarse lumen formation in basal rete. × 240.

differentiation is apparent. The twisting duct with well formed cuticular border occupying a rete peg (Fig. 5) must be regarded as the result of recent differentiation, as the ghosts of the cells which once occupied the lumen are still visible; the plentiful pre-existing sweat ducts have smaller, normal-looking lumina. Lumen formation is to be seen in progress by the splitting asunder of centrally-placed, brightly eosinophilic cells which stain in a manner similar to that of the cuticular lining of normal sweat ducts. Fig. 6 illustrates an area of fine tubular differentiation with small slit-like lumina, some of which are of an easily recognizable acinar type. A less perfect form of differentiation is exemplified by the rete space shown in Fig. 7 which contains eosinophilic material speckled by cell remains; to the dermal side there is a double layer of cells with sharply contoured inner border. The tumour from the calf of the same patient shows a well demarcated lumen lying horizontally in the

mid-rete ; elsewhere are numbers of smaller spaces whose diagnostic significance could be easily overlooked.

The neoplastic generation of sweat ducts is dependent on the formation of splits and spaces in the cell matrices and seems to be accompanied almost always by the necrosis of some cells occupying the sites of future lumina. The basophilic lakes of material are produced by a similar necrobiotic process and are to be interpreted as a very imperfect attempt at tubular differentiation. In them the ghosts of cell borders may still be evident, in a manner similar to that of the well-differentiated duct of Fig. 5. The borders of these lakes are usually sharply demarcated ; where this is not so one usually sees the paler cells with prominent borders, in which presumably greater cell maturity has to some extent hindered the necrobiosis.

In our cases of hidroacanthoma simplex, both verrucose and plane, the underlying sweat coils appear normal in type and position.

Interpretation.

The nature of the matrices.—The neoplasm, parts of which are depicted in Figs. 5–7, has achieved an unusual degree of differentiation well in advance of its companion tumour. The most complete differentiation is to the underside of the surface epithelium, in the rete ridges and in their downward extensions ; within the main mass of the rete the processes of differentiation are less effective and coarse. Behind specimens of this order stands a series of less perfect examples showing tubular differentiation, at times recognizably ductular but whose real nature may be easily overlooked, especially as the matrices are not disposed in narrow duct-like strands. It must be appreciated that all these neoplasms are of one family, only a few members of which are well differentiated. Among the verrucose tumours differentiation is in general poor but sharply demarcated duct-like borders may be seen ; sometimes the opposing wall may be formed by the epidermal cells enclosing the nest. Large spaces containing lakes of basophilic material may however be prominent.

In addition to the morphological data there is a good deal of indirect evidence testifying to the sudoriferous nature of the multifocal nests of these acanthomata. In a small proportion of tumours arising in the sub-epidermal sweat glands the morphology of the cells duplicates that of the matrices of the superficial tumours. In masses of solid epithelium, composed of eosinophilic cells with intercellular bridges, are spaces lined by duct and acinar epithelium containing mostly colloid material ; other spaces however are less perfectly formed and correspond with the necrobiotic lakes seen in the surface tumours. Many of the well differentiated lumina may be large and irregular ; a few may be lined by parakeratotic cells. For our next and very relevant example of a subepidermal tumour we are indebted to Dr. P. W. Harvey.

This tumour had been removed from the neck after an existence of years because of renewed growth. In the deeper corium lies an encapsulated neoplasm showing some sweat differentiation and derived, we think, from the sweat coil. Apart from one portion showing increased nuclear and cellular pleomorphism suggestive of malignant change, the component cells are extremely uniform and strictly comparable with those of the Jadassohn intraepidermal basal cell epithelioma in its most classical form (Fig. 8). The striking finding,

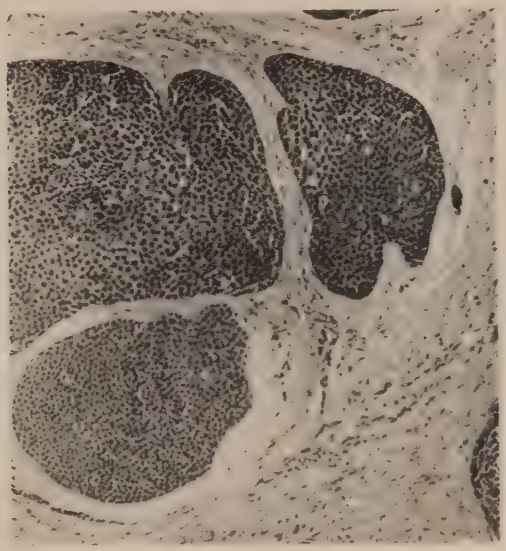

FIG. 8.—Sub-epidermal sweat gland tumour. Small uniform cells. × 120.

however, is the development within the overlying rete pegs of the typical nests of small uniform cells (Fig. 9). These intraepidermal nests must be regarded as arising from the rete itself and the distribution of the neoplasm now corresponds with that of some forms of Paget's disease where a deeply placed glandular tumour is associated with neoplastic activity in the overlying epidermis. This combination of a deep and superficial neoplasia provides a further link in the chain of evidence demonstrating the sudoriferous nature of the multifocal matrices exhibited by the Jadassohn type of intraepidermal basalioma.

Adnexal deviation. The principle of adnexal deviation.—In any neoplastic epidermis the maturation of the cells is disordered ; much of this may represent a deviation of the cells towards an adnexal type, sudoriferous or pilosebaceous. This *adnexal deviation* is a guiding principle to the elucidation of many abnormal cell patterns found in the rete. In hidroacanthomata simplex the new

matrices constitute a sudoriferous metaplasia of groups or large areas of rete cells, which become potentially or actually adnexogenic; the capacity for differentiation is limited to tubular structures of sweat-glandular type. The process is largely confined to the rete though the upper ends of the appendages may be involved.

As we have indicated, differentiation of high quality seems to depend on a more intimate relationship with the stroma, as is brought into being by downward growth. It is not that the adnexal potential of the intraepidermal

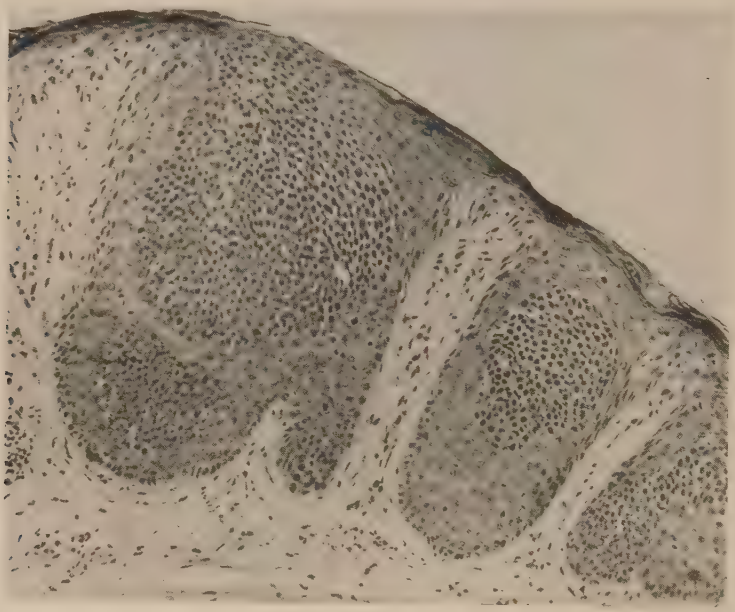

FIG. 9.—Formation of matrix cell nests in rete overlying deeper tumour. × 133.

matrices is necessarily low but their position in the rete is relatively unfavourable. Thus one must regard the elaboration of an adnexogenic matrix as separate from the act of differentiation. Yet, in the absence of tubular differentiation, the matrix cells cannot be expected to remain indefinitely in an immature state and they undergo, as we have seen, a modified type of maturation. Provided the general movement of such cells towards the surface is maintained the resulting epithelium will still be stratified so that in this limited sense the new cells may be regarded as bipotential. Often however, the processes of maturation are more sporadic, leading to individual cell hyalinization or areas of paler cells, or are upset by the necrosis of single cells or groups of cells.

Imperfect deviation.—The neoplasms which we have discussed so far constitute *overt* forms, in that they exhibit matrix cells frankly dissimilar to

normal rete cells. Contrasting with these are others—hidroacanthoma simplex ' imperfectum "—in which the adnexal deviation is minimal. Tumours of this category are of a verrucose build : they merge with and indeed are not separable from certain varieties of flat seborrhoeic wart. Looked at another way the overt verrucose forms may be regarded as an elaboration occurring in a small proportion of seborrhoeic warts from which they are indistinguishable clinically. The plane neoplasms on the other hand clinically resemble psoriasis or chronic eczema. Of relevance with regard to the existence of imperfectly deviated tumours is the fact that in overt verrucose hidroacanthomata areas

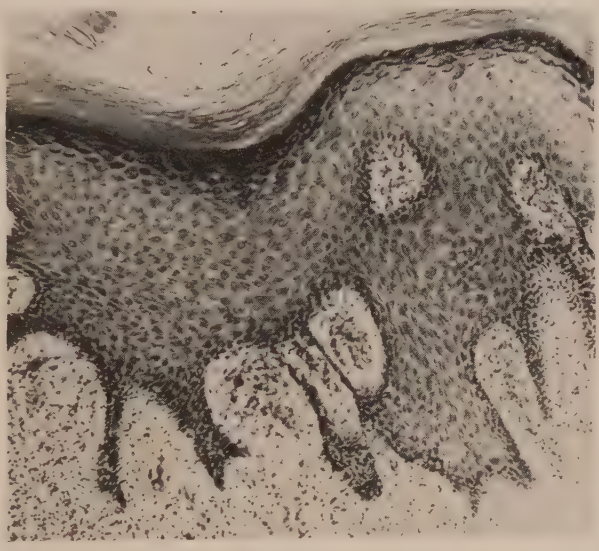

FIG. 10.—Area of non-specific epithelial overgrowth occurring in relation to a verrucose hidroacanthoma. × 120.

of non-specific epidermal overgrowth are found without any adnexal matrices (Fig. 10).

Adnexal deviation as a structural determinant.—The main determinant of tumour structure is the degree of sudoriferous metaplasia, verrucosity being in general inversely related to matrix content. Verrucose simple hidroacanthomata, overt and imperfect, display the same trend towards a papillomatous build as that which characterizes much benign epidermal hyperplasia ; as in the latter there is a primary epidermal overgrowth but accompanied by focal adnexal deviation. The immature matrix cells tend to be very similar morphologically to the small basal cells of the normal rete. The plane forms comprise a large scale replacement of the rete by proliferat ing cellsof adnexal type ; they therefore do not include examples of hidroacanthoma simplex imperfectum. Thus, corresponding to verrucose and plane varieties of tumour one can recognize two main histological types, epidermo-adnexal and adnexal.

The differences between the two are well brought out by the accompanying table. Of course, not all tumours correspond to the one or other extreme of structural pattern ; some are of an intermediate plano-verrucose build with a suitably modified histology.

Benign Hidroacanthoma Simplex.

	Epidermo-adnexal type.	Adnexal type.
Clinical features	Flat seborrhoeic wart	Scaly, slightly raised plaque.
General build	Verrucose	Plane.
Arrangement of matrices	In nests	Diffusely and in nests.
Morphology of immature matrix cells	Small basal type with scanty cytoplasm	Plumper cells with round or spindle nuclei.
Quality of differentiation	Poor	Poor or good.
Areas of " imperfect " neoplasia	Often prominent.	Minimal.
Imperfectly deviated tumours	Existent	Non-existent.

Classification on the basis of adnexal deviation.—The fundamental fact about the present group of acanthomata is the presence of a sudoriferous metaplasia : this surely must form the basis of their classification and not speculation as to whether the component elements are of basal or squamous type or both. The matrices constitute neoplastic primordia capable of unidirectional adnexal differentiation. The term " hidroacanthoma simplex " therefore provides a more precise and natural designation for these tumours than the existing nomenclature.

Relationship to other neoplasms.

We recognize two other major classes of sudoriferous acanthomata which it is hoped to discuss in subsequent articles. These are found in regions of the skin bearing sweat glands of an apocrine or semi-apocrine status. Many would doubtless be included in the large series of cases (40) quoted by Haber (1954) in his paper on intraepidermal epithelioma (Borst-Jadassohn).

The simplex tumours have been reported only infrequently in the literature. A good example of a verrucose hidroacanthoma simplex is the second tumour (growing beneath the arch of the ribs) mentioned by Jadassohn (1926). Of the three tumours reported by Sims and Parker (1949) only the second (from the abdomen) would be acceptable as belonging to the simplex group. We ourselves have only twelve examples of this rare type of sudoriferous reaction in the rete, at least in its fully developed and benign forms. The favourite site for these neoplasms is the trunk, on its ventral or lateral aspects, and the limbs with the exception of the hands and feet.

Malignant Hidroacanthoma Simplex.

Malignant hidroacanthoma simplex is a rare neoplasm of the trunk and extremities : like their benign counterparts they are less common in specialized sites such as the face or on the hands and feet. With some exceptions they

onform to the general rule of slow growth and of limited and long-delayed nvasive habit shown by epitheliomata in these regions. They are onveniently divided into (i) Invasive cancer, and (ii) *In situ* cancer. Among oth varieties one can recognize, as in benign hidroacanthoma simplex, two ain types, namely the epidermo-adnexal and the adnexal.

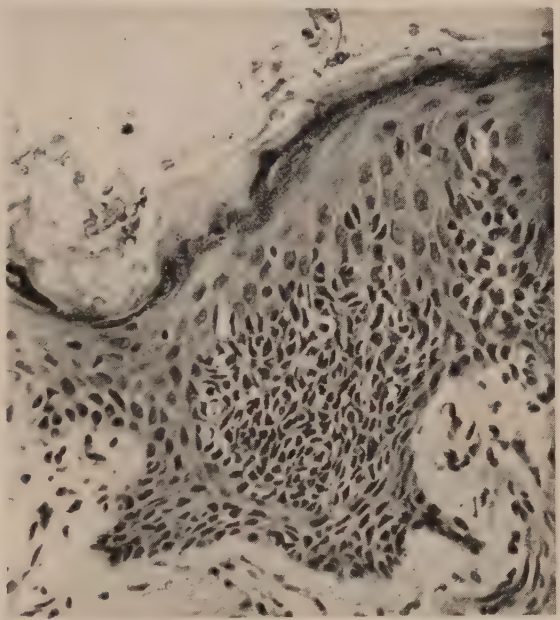

FIG. 11.—Malignant hidroacanthoma simplex. Nest of matrix cells in border zone. × 330.

Invasive Cancer.

We have two examples of this. The first is from the back of the left thigh of a man aged 66 years, which, interestingly enough, had been labelled " epithelioma on seborrhoeic wart ". The tumour formed an oval about 4 cm. long. It had a slightly raised border zone with a finely lobular surface, and a large granuloma-like central mass lying a little eccentrically and occupying about three-fifths of the tumour length.

Histologically, the border zone is seen as a somewhat verrucose epidermis with a thickened scale ; in this moderately acanthotic portion of the rete are the characterizing nests of small cells (Fig. 11) and in some of these are a few larger, cancerous-looking elements. Approaching the main cancerous area the changes in the rete become intensified, notably by the wide spacing of the cells in many of the nests—intercellular oedema.

In the central plateau the histology is that of a " keratinizing squamous cell carcinoma ". In a plentiful fibrocellular stroma, containing very few inflammatory cells, lie erratically disposed strands of angulated cells ; the latter are

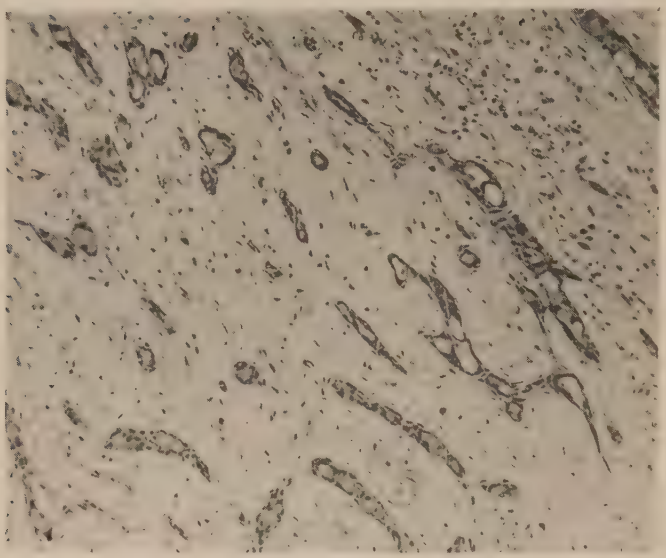

FIG. 12.—Invasive carcinoma. Narrow strands of cells with duct formation. × 167.

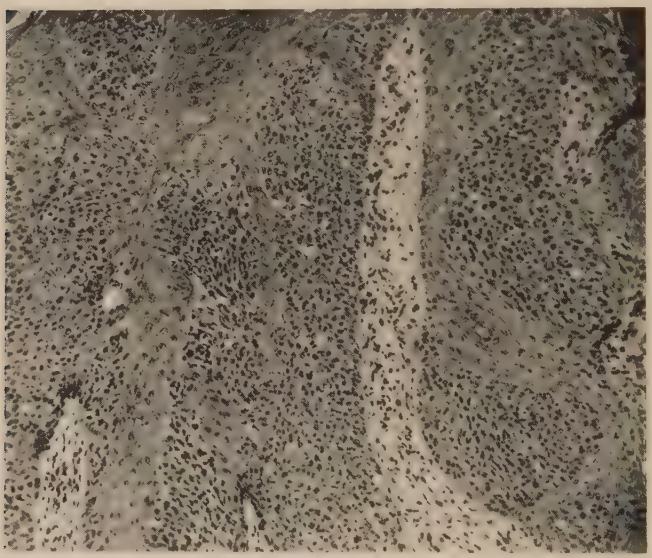

FIG. 13.—Large areas of cancerous matrix cells within the rete. Surviving framework of epidermal cells. Plane hidroacanthoma simplex of right leg. × 120.

mostly small and enclose areas of larger cells and cavities containing cornified and hyalinized elements. Most striking is the number of strands which are long and thin and which contain narrow duct lumina in which are the remains of broken down and hyalinized cells. The bordering cells average about two layers and many of the new lumina have a thick cuticular lining of eosinophilic material (Fig. 12).

Our second case differs from the preceding in being an initially plane lesion. This neoplasm was removed from the right leg of a 72-year-old man. Histologically there is an intraepidermal carcinoma, part of which has become invasive. In the non-invasive lateral portions the rete is thickened by areas of new cells, often arranged in circumscribed nests, which contrast with the surrounding epidermal cells as they are somewhat smaller and have less brightly eosinophilic cytoplasm (Fig. 13). They differ from the equivalent cells of benign neoplasms in their somewhat increased nuclear and cellular pleomorphism and in the presence of plentiful mitoses. In a few nests the cells have a more ample cytoplasm with some further reduction in eosinophilia.

In the invasive portion of the tumour relatively narrow columns of epithelium of adenocarcinomatous type lie in a fibrocellular stroma. The individual cells are similar to those of the intraepidermal nests but are more loosely arranged owing to some break-up of the intercellular bridges. Lumen formation is in general defective but is indicated by the presence of narrow spaces lined by a sharply demarcated layer of cells. Loss of surface epithelium has led to an ulcerated area over part of the tumour. The underlying sweat-coils are unaffected.

Interpretation.

Each invasive cancer is easily recognized as the malignant homologue of a benign hidroacanthoma simplex ; the structure of the non-invasive portions is typical enough. In the tumour illustrated in Figs. 11 and 12 the invasive epithelium has adopted a mixed surface and adnexal character : this was to be anticipated from the verrucose build of the non-invasive peripheral regions and from the type of matrix cell in the intraepidermal nests (epidermo-adnexal type). A routine diagnosis of keratinizing squamous cell carcinoma would be inaccurate on two counts. First, it ignores the obviously sudoriferous nature of the numerous thin columns of epithelial cells and of their enclosed canals. Second, though the cancerous matrix cells have produced, in addition to the tubules, masses of keratin-like material they have done so by a simplified maturation process ; there is no intermediate keratohyalin layer and the matrix cells cannot therefore be regarded as being fully epidermal in character. Further, it seems that much of the eosinophilic substance in the hyalinized cells is to be identified with the cuticular lining of sweat ducts rather than with

keratin, though all transitions or mixtures between the two may exist in fact. That it is the invasive epithelium which has differentiated into sweat ducts again draws attention to the role of the stroma in facilitating differentiation.

Our second case of invasive cancer contrasts with the foregoing in belonging to the adnexal series. This is apparent in the cell matrices of its lateral portions where the neoplasia is still confined within the rete : not surprisingly therefore the invasive cancer is of an adenocarcinomatous type and lacks the masses of keratin-like material so prominently displayed by the primarily verrucose tumour.

FIG. 14.—Hidroacanthoma simplex from upper arm. *In situ* cancer with marked cell pleomorphism. Illustrates involvement of upper part of follicle. × 80.

In situ *cancer.*

Small numbers of malignant hidroacanthomata exist in which the rete maintains a close structural resemblance to that of the normal epidermis. These neoplasms exhibit a low-grade malignancy. Variations in the size of the cells and in their arrangement are evident in places : the nuclei also are relatively hyperchromatic and the number of mitoses may or may not be increased above the normal. The granular layer is largely lost and the stratum corneum is replaced by parakeratotic cells, often forming a compact layer but which may be mixed with or underlie a hyperkeratotic scale. Small

numbers of hyalinized cells are present in the rete. With increasing cell pleomorphism the latter tend to increase and the scale becomes increasingly defective.

In other *in situ* cancers there is a widespread appearance of a new type of cell in the rete but a framework of normal epidermal cells persists, especially in the upper rete, so that the granular and horny layers tend to be comparatively well preserved. The new matrix cells contrast with the epidermal cells in their paler cytoplasm ; in some of the cells the latter may appear almost empty though the heavily contoured cell borders remain as do the inter-cellular bridges. Mitoses are few. Some clumping of the nuclei is evident. More florid examples are found in which there is marked anisocytosis and anisonucleosis in association with abundant bizarre and clumped nuclei (Fig. 14). Under these conditions the replacement of the rete by matrix cells may become almost total. The upper ends of the appendages are involved in the neoplasia to a limited extent.

Interpretation.

Members of our first sub-group of *in situ* cancers are to be regarded as completing the epidermo-adnexal series of hidroacanthoma simplex. It is tempting to regard the rete in this class of tumour as being composed of epidermal cells ; they are normally accepted as such. Against such a simple interpretation is the nuclear hyperchromatism, the absence of an upper zone of large epidermal cells, the loss of the granular layer and the formation of a compact parakeratotic scale. These epidermal changes may be regarded as comprising a relatively imperfect measure of adnexal deviation, but comparable to that seen in the nests of benign verrucose lesions. It must be remembered that, morphologically and embryologically, the cells of normal sweat ducts are close relatives of those occupying the general mass of the lower and middle rete. These similarities might be expected to extend into the neoplastic field. The majority of eccrine sweat glands arise relatively late in foetal life, at a time when the epidermis is beginning to assume adult characters, as judged by the appearance of keratin. In this respect the " squamous metaplasia " of sweat ducts seen in some inflammatory conditions is noteworthy ; Weidman (1924) found marked squamous metaplasia in multiple sweat ducts in biopsies taken from vaccinia and erysipelas lesions.

Our second sub-group of *in situ* cancers completes the adnexal series of hidroacanthoma simplex. The type and distribution of the matrix cells in the rete are similar to those of the other two variants in the series. The matrix cells are at first situated in the deeper rete so that their impact on the surface scale is delayed for some time. They display a variable and often marked degree of cellular and nuclear pleomorphism, contrasting thereby with their

epidermo-adnexal equivalents ; the matrix cells in tumours of the adnexal series are always more pleomorphic than those in corresponding epidermo-adnexal forms.

Primary and consecutive cancer.

Theoretically, cancerous examples of hidroacanthoma simplex might arise as malignant neoplasms *de novo* or as a malignant degeneration of initially benign tumours ; on this basis one would recognize two classes of carcinoma, primary and consecutive. Any such subdivision could never be regarded as absolute since there are degrees of benignity and the initially benign phase of consecutive cancers may be only relatively so. Nevertheless the concept is of value in practice.

In both our invasive cancers the structural patterns of benign hidroacanthoma simplex are clearly manifest in the non-invasive portions of the rete : only the number of mitoses and the moderate increase of pleomorphism seen in some areas indicates the cancerous trend. It would be legitimate to regard these two tumours as examples of consecutive cancer. Their theoretical importance is thus considerable since they clearly show that :

(i) Invasive cancer can supervene on an intraepidermal epithelioma of Jadassohn type. Haber and Seville (1953) stated that they had never seen a case of intraepidermal epithelioma which had penetrated through the basal layer.

(ii) The invasive columns can adopt a tubular form of unmistakably sudoriferous nature.

As in benign hidroacanthoma simplex, some of the intraepidermal nests, usually those in the upper rete, are composed of larger and more mature cells but in both varieties there is always an excess of immature cells. The invasion of the underlying tissues must be attributed in large measure to a rapid accumulation of these immature cells which can no longer be carried intra-epidermally.

Most of the *in situ* cancers are probably malignant from the outset or from a very early stage. One indication is the preference shown by those of epidermo-adnexal type for a plane rather than a verrucose build. In these low-grade cancers there is only a slow production and therefore no great accumulation of immature matrix cells ; production is balanced by maturation rate so that a simplified stratified epithelium results with a surface layer of parakeratotic cells. The new epithelium has largely ceased to be epidermal ; it is only epidermo-mimetic.

We have only three examples of *in situ* cancer belonging to the adnexal series. Two of them have an almost identical histological picture ; the matrix cells in the only moderately acanthotic rete have a fairly ample cytoplasm and

toutly delineated walls ; many of the nuclei contain sizeable nucleoli. There re no nest-like accumulations of immature cells ; the matrix cells are effectively ntegrated with the epidermal cells, maturing with them as they move towards he surface. In so doing they emphasize the near-relationship of the idradnexal and the epidermal cells, in the physiological as well as in the natomical sphere. Our third example shows much greater nuclear bnormalities suggesting a high degree of malignancy (Fig. 14). Here again he *in situ* course must be related to the general high level of cell maturity ; he matrix cells have a very plentiful cytoplasm though relatively pale as if the osinophilic element had been diluted. The large and clumping nuclei must e attributed to nuclear division in these relatively mature matrix cells. Even n this last neoplasm the cancerous epithelium continues to function as though t were of a true surface type. All three of these neoplasms probably represent rimary cancer. It seems that the prolonged *in situ* course of the primary ancers, both of epidermo-adnexal and adnexal type, depends on their ability o maintain the maturation of the matrix cells at a level commensurate with roduction.

Bowen's disease : Relationship to the Jadassohn intra-epidermal basalioma.

Primary cancers of the adnexal series typify Bowen's disease. Only a proportion, however, of the neoplasms reported as Bowen's disease, if a substantial one, belong to the hidroacanthoma simplex group. Jamamoto (1925) described as Bowen's disease two such cases, one neoplasm being from the sternal region and the other from the left thigh ; both were of several years' duration. He found particularly striking the almost total preservation of the intercellular bridges, an attribute which is so characteristic of the matrices of hidroacanthoma simplex. Of some importance is the fact that the low-grade primary cancers of epidermo-adnexal type may be part of a systematized Bowen syndrome. Such neoplasms will usually have been reported as intraepidermal carcinoma.

The common nature of many classical Bowen and Jadassohn lesions is strongly supported by both morphological and clinical evidence. Both types of lesion tend to be multiple and the duration of either may extend over many years. Their clinical appearance is identical—sharply demarcated, flat or slightly raised, partly scaling plaques, sometimes forming gyrate or odd-shaped figures. Only rarely are these lesions found on the face, where they seem to occur in the region of the lids and canthi.

Thus, some Bowen cancers emerge as primarily malignant equivalents of the Jadassohn type of intraepidermal epithelioma. The two cases of multiple neoplasms reported by Fraser (1928) as Bowen's disease are important as they fall into an intermediate category. The lesions were non-invasive and of low

grade malignancy: many of them were examined histologically. The cells tended to arrange themselves into "alveoli lined by compressed epithelium"; Fraser's Fig. 2 shows a multifocal Jadassohn type of lesion with very even cells and only occasional clumped nuclei. The one large plaque which was broken up into small nodules "like a hepar lobatum" suggests a seborrhoeic wart and may well have represented an imperfectly deviated hidroacanthoma simplex.

Summary.

Our purpose has been to draw attention to the existence of sudoriferous metaplasia in a number of superficial neoplasms of the skin. The neoplastic cells arise by an adnexal deviation of the rete cells; the matrices which they form represent neoplastic primordia in which, under suitable conditions, differentiation into sweat glandular structures will occur. The structure of individual tumours is linked to the degree of adnexal deviation. Six structural variants can be recognized, two being benign and four malignant.

In their histology many examples of benign hidroacanthoma simplex correspond with the intraepidermal basal cell epithelioma as classically described by Jadassohn. Among the tumours generally classed as seborrhoeic warts are a few which represent *formes frustes* of hidroacanthoma simplex. The cancers include examples of intraepidermal carcinoma and of Bowen's disease. Reasons are advanced for the prolonged *in situ* course of many of the latter.

Acknowledgments.

We wish to acknowledge our gratitude to Dr. Louis Savatard for the loan of many slides; to Professor A. C. P. Campbell for much helpful advice and criticism; to Miss K. Hughes and Mr. J. Hodkinson for the photographs; and to Mr. P. Morewood for the preparation of slides.

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NORTH OF ENGLAND DERMATOLOGICAL SOCIETY

Leeds, June 1956.

Calcinosis Cutis Circumscripta.—Dr. Clifford Stuart.

A woman aged 38.

History.—For the past ten years she has had lesions on the hands which she believed to be warts.

On examination.—There were four raised, round, hard, sharply demarcated lesions of a slightly yellow colour, varying from 5 mm. to 1 cm. in diameter. The surface was slightly rough. There was one on the ulnar border of each hand and the two others were on the fingers of the right hand. The rest of the skin was normal except for a little perniosis of the legs. There was no scleroderma.

Histology.—There is a well circumscribed lesion in the corium containing amorphous granules and larger masses of calcium separated and surrounded by thin strands of reactive connective tissue. The skin appendages are atrophied. The calcium deposits have evoked neither an inflammatory nor a foreign-body reaction. The epidermis shows hyperkeratosis and loss of the rete pegs.

Investigations.—Serum calcium 9·2. Serum inorganic phosphate as phosphorus 2·5 mg.%. Serum cholesterol 200 mg.%. Skiagram of the hands shows opacities at the sites of the lesions, but no bony changes.

Sclerosing Lipogranuloma.—Dr. Eric Ritter.

A woman aged 61 first noticed a small lump at the outer side of the right eye about one year ago. Slight infiltration spread over the upper eyelid and a little below the eye. The lesion was almost painless.

On examination.—There is firm induration of the skin and subcutaneous tissue about $1\frac{1}{2}$ cm. across lateral to the right outer canthus, with a band-like infiltration spreading into the outer part of the upper and lower lids. The overlying skin is slightly yellowish.

Past history.—Since 1949 she has attended the Ear, Nose and Throat Department frequently with recurrent nasal polyps and sinusitis. Partial ethmoidectomy was done in 1949, and left Caldwell-Luc operation in 1950. Polypi had been removed on several occasions. There is a history of ecchymosis of the right orbit after one of the nasal operations.

Family history.—Nothing of note.

General medical examination.—Nothing of note. Skiagram of chest: normal. W.R.: negative. Blood count: normal. Urine: normal. Mantoux: positive, 1 in 1,000.

Histology (September 1955).—The specimen consists of fibrous and fatty tissue infiltrated by a variety of cells. With the exception of one large collection of lymphocytes the infiltrate consists chiefly of fibroblasts and histiocytes. A few of the latter are of the foamy type, with an occasional multinucleated cell. Small numbers of lymphocytes and polynuclears are also present. A number of fairly large, round, apparently empty spaces are present throughout the section. Some of them are surrounded by histiocytes, and were presumably occupied by fat but this was not proved on account of the small size of the biopsy, the whole of which was processed and cut serially. The appearances are consistent with a chronic granuloma, related in some way to fatty tissue or possibly fat debris derived from meibomian secretion.

Comment.—This seems to be the condition described by Anning (1951). The history of preceding trauma with ecchymosis is of note.

Reference.

Anning, S. T. (1951) *Proc. Roy. Soc. Med.*, **45**, 101.

Macrocytic Anaemia associated with Dapsone Treatment.—Dr. A. J. E. Barlow.

A woman aged 48.

History.—This patient has suffered from dermatitis herpetiformis for five years and was given dapsone 100 mg. daily from 6 April 1956, her blood count at that time being normal. The skin cleared completely in a few days and she became symptom-free for the first time for five years. In the first week in May she felt ill and became dyspnoeic on exertion. The haemoglobin had then dropped to 80%, the RBC being 4·02 million with some macrocytosis. The pathologist reported the picture as suggestive of pernicious anaemia. A fractional test meal showed acid-fast achlorhydria. Dapsone was stopped on 11 May, and by 14 May her haemoglobin had fallen to 60%, the RBC to 3·59 million. The sternal marrow on this date showed no megaloblastic reaction.

By 4 June, with no further treatment, her haemoglobin had returned to 94%.

BOOK REVIEWS

Von Recklinghausen's Disease.*

This small monograph presents the results of an investigation into the genetic aspects of multiple neurofibromatosis carried out at the University of Michigan. Although the book is described as a clinical, pathological and genetic study, the authors do not attempt to provide detailed descriptions of the various physical abnormalities which may occur in multiple neurofibromatosis, and the clinical section is mainly concerned with the frequency of different manifestations in the authors' series. There is a short chapter on pathology which is adequately illustrated and documented. The remainder of the book contains case summaries of the 110 families and 20 single cases investigated, followed by a genetic interpretation of the material.

At first sight this seems a rather indigestible collection of factual material but this presentation is chosen deliberately by the authors in order that "later investigators can return to it with new techniques and approaches and extract additional information". The statistical analysis and the final conclusions derived from it gain greatly from the large scale of the survey. R. W. G.

Cosmetic Dermatology.†

The first sight of this large book made me wonder how it was possible to expand the subject so much, but a look at the chapter headings showed that the authors had included much that is not usually found in books on this branch of dermatology. An opening chapter on the history of cosmetic dermatology is followed by several on the anatomy and physiology of the skin. Succeeding ones treat of every alteration of the skin, either structural or functional, in which an unaesthetic appearance is prominent. Consequently one reads about keratodermia punctata, epidermodysplasia verruciforme etc., affections that a dermatologist does not usually think of as cosmetic blemishes. In fact one can learn much dermatology before reaching the chapters on cosmetic therapy which occupy less than half the book. Almost everything one can think of is included except a few recent methods that have not yet stood the test of time—perhaps the authors think that they will not.

Nearly all the illustrations are good, but a few could be improved in subsequent editions. This book is perhaps unique in its scope and will undoubtedly become a necessary part of the library of Spanish-speaking dermatologists. G. W. B.

Pemphigus and Duhring-Brocq's Dermatitis.‡

After reviewing the subject the author presents his findings in 228 patients with bullous disorders, 176 of whom had pemphigus foliaceus, the most common type in Brazil. The essential feature of pemphigus is acantholysis, and he thinks that a

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* *A Clinical, Pathological and Genetic Study of Multiple Neurofibromatosis.* Frank W. Crowe, M.D., William J. Schull, Ph.D., James V. Neel, M.D., Ph.D. Oxford: Blackwell Scientific Publications. Pp. 181. Illus. 15. Price 36*s*.

† *Dermatología Cosmética.* Marcial I. Quiroga and Carlos F. Guillot. (1955) Buenos Aires: "El Ateneo". Pp. 686. Illus. 260.

‡ *Pênfigo e Dermatite de Duhring-Brocq.* Benjamin Zilberberg. (1955). São Paulo. Pp. 175. Figs. 89.

positive Tzanck's test on the contents of a recent bulla is even more reliable than serial sections of a whole bulla, as occasionally an intraepidermal bulla is seen in dermatitis herpetiformis. In pemphigus vulgaris there are also monstrous cells which are not present in pemphigus foliaceus or Senear-Usher disease. He points out that, probably from the trauma of biopsy, an edge of the section may become detached and the line of cleavage is then at the level of a bulla if one were present. Dermatitis herpetiformis is much less uncommon than pemphigus, and the false Nikolsky sign, subepidermal detachment by trauma, is restricted to the severe monomorphous type which may be fatal but never turns into pemphigus.

The book is well printed and the photomicrographs are excellent. There is a 14 page summary in English. G. W. B.

Pharmacology (1956).*

Modern pharmacology is vitally interesting to all who practice medicine, whatever their specialty, but it is not easy to keep up to date with advances in this enormous subject. The new edition of *Recent Advances in Pharmacology* is most welcome, as it provides excellent reviews of many new therapeutic agents. The presentation is admirable with neatly headed paragraphs in which the setting out of data and the discussion are easy to follow. We find chapters on the adreno-cortical steroids, the newer antibiotics, the anticoagulants, the physiological agents such as histamine, serotonin, adrenaline and nor-adrenaline and the neuromuscular-blocking drugs. Radiation hazards are discussed (rather beyond the range of pharmacology) and nucleotoxic drugs and anti-emetics such as chlorpromazine.

Naturally one would not expect any particular reference to dermatology, but one might regret the omission of any reference to lupus vulgaris when the treatment of non-pulmonary tuberculosis is discussed, in view of the fact that dermatologists led the field in the effective treatment of tuberculosis. Nor would most dermatologists allow that antihistamines by mouth relieve the itching of eczema and pruritus ani, as is stated on page 106 in support of the role of histamine in itching. These minor criticisms do not really detract from the general excellence of this very useful book.

G. C. W.

Skin Surgery†

This book is designed to fill a gap in dermatological training by well illustrated descriptive articles from seventeen different authors who are acknowledged experts. Cold surgery, electrosurgery and certain special techniques such as chemosurgery of cutaneous cancer, dermabrasion and cryosurgery are all discussed in detail with useful illustrations.

The only criticism which can be made is that Chapters 4, 5 and 6 would be best found in a book on plastic surgery. Skin grafting, oral plastic surgery and surgical treatment of advanced visible cancer are surely in the realm of the plastic surgeon rather than the dermatologist.

This book is beautifully produced and all the diagrams and illustrations are good. It should be of distinct interest to all dermatologists. R. M. B.

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* *Recent Advances in Pharmacology* (1956). By J. M. Robson and C. A. Keele. 2nd ed. London: J. & A. Churchill Ltd. Pp. 500. Illus. 66. Price 40*s*.

† *Skin Surgery*. Ervin Epstein (1956). London: Henry Kimpton. Pp. 228. Illus. 242. Price 56*s*.

CURRENT LITERATURE

PROTECTIVE REGIME WITH PROLONGED HYPNOTIC SLEEP IN THE TREATMENT OF CERTAIN DERMATOSES. V. A. Arutunov and S. M. Kaltgrad. (1956) *Vestnik Ven. Derm.* (*Moscow*), **1**, 8.

An analysis of three years' experience: only local treatment apart from prolonged hypnotic sleep. Apparent recovery rate highest in the very numerous warts group (11 out of 12 patients, no specific mention of local treatment here) and pruritus (13 out of 19): lowest in lichen planus (failure or only partial improvement in 5 out of 6): apparent recovery in only 7 out of 29 with neurodermatitis and in approximately 50% of the remaining two groups—eczema and psoriasis. Of the total 286 patients 207 were discharged within a month and all but one within 10 weeks: there were 9 failures. M. S. S.

SOAP AND THE SKIN WITH AN INVESTIGATION INTO THE PROPERTIES OF A NEUTRAL SOAP. I. Martin-Scott and A. G. Ramsay. (1956) *Brit. med. J.*, i, 1525.

A neutral soap was investigated. It was found that after skin had been washed with it the "skin-fat factor" (which indicates the composition of a sample of skin fat) and the pH of the skin remain unaltered. In a clinical trial the soap was well tolerated by about 100 patients suffering from subacute eczematous dermatitis of various types. S. T. A.

MULTIPLE CUTANEOUS CARCINOMA AFTER CREOSOTE EXPOSURE. N. Leucon. (1956) *New Engl. J. Med.*, **254**, 520.

The presence of five primary carcinomas on the face, with keratotic and pigmentary lesions on exposed skin elsewhere is reported in a man aged 64 who had been painting with creosote for three years. A. D. P.

DISSEMINATED HERPES ZOSTER COMPLICATING CHRONIC LYMPHATIC LEUKAEMIA. G. P. Rodnan and G. W. Rake. (1956) *New Engl. J. Med.*, **254**, 472.

Zoster was followed eight days later by a widespread varicelliform eruption in a man with lymphatic leukaemia.

Electron microscope studies of fluid from disseminated vesicles disclosed particles indistinguishable from those previously observed in zoster, thus suggesting that in such cases the same virus is responsible for the two conditions.

A. D. P.

VALUE OF TREATMENT IN REITER'S DISEASE. W. Fowler and G. H. Knight. (1956) *Brit. J. vener. Dis.*, **32**, 2.

Clinical material was 73 male and 2 female patients aged from 20 to 55 years. The effect of various types of treatment is assessed and no evidence found that any form of therapy at present in use has any influence upon the course of the disease. W. G. A.

KERATODERMIA BLENORRHAGICA. J. Malcolm Cameron. (1956) *Brit. J. vener. Dis.*, **32**, 7.

Two cases are reported of Reiter's syndrome with keratodermia blenorrhagica as an associated skin lesion. In neither case was there any history of previous gonococcal infection. The skin lesions were present only on the soles of the feet, and balanitis circinata noted in both patients, while aphthous ulcers in the mouth were present in one. Culture of the pus from the skin lesion of one patient yielded a coagulase-positive *Staphylococcus aureus*. Treatment with aureomycin appeared to benefit. W. G. A.

GENERAL PARALYSIS OF THE INSANE. W. D. Nicol. (1956) *Brit. J. vener. Dis.*, **32**, 9.

No one who is familiar with the vast literature devoted to neurosyphilis can fail to be impressed by the infrequency with which GPI now claims attention in current medical journals. The reason for this is not that man has become more continent or a less lascivious animal, but rather that new therapeutic advances have robbed syphilis of its more dangerous sequelae. Assuming

that the average incubation period of general paralysis is 10 to 15 years, the next few years should provide us with the answer about the efficacy, or otherwise, of the new therapeutic measures as from 1946. W. G. A.

EXPERIMENTAL STUDIES TO DEVELOP LOCAL PROPHYLACTIC AGENTS AGAINST SYPHILIS. R. C. Arnold and John C. Cutler. (1956) *Brit. J. vener. Dis.*, **32**, 34.

Experimental studies of the effectiveness of various agents in local or systemic prophylaxis against syphilis are reported. No attempt has been made to determine the relative effectiveness of the prophylactic preparations tested, but the high degree of effectiveness of locally applied solutions of Fumerane, or of parenteral penicillin, is clearly indicated. A table, which tabulates the prophylactic agents, including combinations of preparations, shows the number of animals protected in relation to those exposed for various intervals of exposure. (In view of the effectiveness of modern therapy in syphilis the question of prophylaxis is debatable because, unless it can be thoroughly relied upon, it may well be fraught with danger.) W. G. A.

COMPLEMENT-FIXATION TITRES IN TERTIARY LYMPHOGRANULOMA VENEREUM. Julius Goldberg and Leon Banov, Jr. (1956) *Brit. J. vener. Dis.*, **32**, 37.

The authors state that patients with tertiary lymphogranuloma venereum continue to maintain circulating complement-fixation bodies against the virus for as long as 27 months, even after clinically satisfactory antibiotic treatment. Diminishing complement-fixation titres cannot be used to establish a retrospective diagnosis of the disease even after clinically successful therapy with the broad-spectrum antibiotics. W. G. A.

INVESTIGATION OF THE ANTIHISTAMINE-LIKE ACTION OF MEPACRINE. E. Nagy and L. Kocsar. (1956) *Derm. Wschr.*, **133**, 265.

Light protection as stipulated by Page is not considered to be the only reason for the therapeutic effect of mepacrine in lupus erythematosus. In human experiments the authors demonstrated an increase of 17-ketosteroid excretion through mepacrine and in animal experiments a protection against histamine shock. In other animal experiments they showed that mepacrine was capable of reducing the degree of oedema produced by intraperitoneal injection of egg protein into rats. This result is similar to that obtained by cortisone and ACTH and it is considered that antihistaminic action of mepacrine results from mobilization of cortisone.

W. G. T.

HISTOPATHOLOGICAL INVESTIGATION OF THE TUBERCULIN REACTION. A. Reichel-Bergmann. (1956) *Derm. Wschr.*, **133**, 269.

In view of the difference of opinion about the nature of the tuberculin reaction experiments were carried out on 10 guinea-pigs and 10 patients suffering from lupus vulgaris. The injection of old tuberculin produced papules. These were excised, in the former after 3 days and 6 days, in the latter after 9 days. In each case typical tuberculous granulation tissue was demonstrated.

W. G. T.

CLINICAL AND HISTOLOGICAL PECULIARITIES IN A SPORADIC CASE OF ECTODERMAL DYSPLASIA WITH ANIDROSIS. O. Braun-Falco and W. W. Gürtler. (1956) *Derm. Wschr.*, **133**, 289.

In view of the great variety of ectodermal structures a multitude of syndromes resulting from dysplasia are to be expected. All the same most seem to fall into an anidrotic group along with hypodontia and hypotrichosis, and a hidrotic group with hypoplasia of the nails and hair and without dysplasia of the sweat glands. It is surprising how rarely other ectodermal structures such as the central nervous system and the lens are involved. Amongst 100 cases there are only 2 showing oligophrenia and congenital cataracts and 3 with nervous degeneration of the Friedreich type. There is a detailed description of a case with absent eccrine sweat glands, hypotrichosis, hypodontia, deformity of the nose, dysplasia and diminution in number of sebaceous glands. Significant was the absence of apocrine sweat glands and there was evidence of a " forme fruste " of Friedreich's ataxia. The abnormalities are considered to be of congenital origin and to have developed before the 18th week. There was no evidence of congenital syphilis.

W. G. T.

PIGMENTATIO LONGITUDINALIS STRIATA UNGUIUM. H. Langhof and W. Schwenke. (1956) *Derm. Wschr.*, **133**, 297.

Pardo-Costello states that this condition, though common in negroids and asiatics, is rarely seen in white patients and the literature mentions only 10. A further case is added. A woman of 59 developed longitudinal brownish band-like discoloration of all nails at her menopause. In addition there was dirty brown pigmentation of the knee and elbow areas and hyperpigmentation of the circumanal region and the labia minora. The labia majora were depigmented. Addition of histidin and tyrosin to the urine produced a brown deposit, not seen in the urine of normal persons, and the patient was thought to produce an enzyme changing tyrosin and histidin into a brown pigment.

There was no evidence of Addison's disease, though the importance of the changes described as early symptoms of this disease is stressed. W. G. T.

VACCINATION IN THE PREVENTION AND TREATMENT OF OTHER DISEASES. AN HISTORICAL STUDY. W. Schönfeld. (1956) *Derm. Wschr.*, **133**, 313.

Ever since the success of vaccination against small-pox attempts have been made to prevent or treat a variety of diseases by this method. During the 18th and 19th century it was used against plague, measles, scarlet fever and syphilis. Later whooping cough and mycosis fungoides were so treated and despite the doubtful results the treatment has persisted into present times. It has been recommended in the treatment of pemphigus vulgaris, despite the fact that it has been known to precipitate this disease and on the basis of a crossed herpes-vaccine immunity in recurrent herpes simplex. The author dismisses this treatment as not justifiable in either of these conditions. W. G. T.

BERYLLIOSIS: A CASE REPORT. I. B. Sneddon. (1955) *Brit. med. J.*, **i**, 1448.

After trimming 2% beryllium-copper alloy strip for 3½ years a girl developed sarcoid-like granulomata on her hands and forearms. She was found to have a pulmonary granulomatosis clinically similar to delayed chemical pneumonitis due to beryllium. The patient had eczematous hypersensitivity to beryllium shown by positive patch tests to high dilution of beryllium salts and a delayed sarcoid reaction in the skin used for patch tests. B. A. T.

FAVUS: A REPORT OF SEVEN RELATED CASES. J. Hansell and B. M. Partridge. (1955) *Brit. med. J.*, **i**, 1510.

The diagnosis and identification of the source of infection of seven cases of favus in the London and Kent areas. B. A. T.

THE INHERITANCE OF PORPHYRIA. G. Dean and H. D. Barnes. (1955) *Brit. med. J.*, **ii**, 89.

Of thirteen porphyric families investigated, the family tree of one is presented. The 236 members of all the families demonstrated porphyria in its acute form, in its chronic cutaneous form, or as a symptomless porphyrinuria. They are different manifestations of the same inherited disorder, the type changing in some instances.

50% of the children of a poryphyric family will inherit porphyria, the sex incidence being approximately equal. Porphyria is a Mendelian dominant and is not sex-linked.

Cutaneous manifestations are more pronounced in men but acute attacks are more common in women.

It is important to trace the genealogical tree in a porphyria case and to investigate the other members of the family. B. A. T.

TRICHOPHYTON SULPHUREUM RINGWORM. D. Sharvill. (1955) *Brit. med. J.*, **ii**, 415.

A case of tinea circinata is described in a 10-day-old infant; the 19-year-old mother suffered from tinea capitis and tinea unguium. Three nurses attending the baby were infected. B. A. T.

MALIGNANT CHANGE ARISING IN TISSUES AFFECTED BY HERPES. R. Wyburn-Mason. (1955) *Brit. med. J.*, **ii**, 1106.

A series of 26 cases of herpes zoster in which the affected areas of skin subsequently developed malignant changes, either basal- or squamous-celled carcinoma. B. A. T.

DIAGNOSIS AND TREATMENT OF PEMPHIGOID. I. B. Sneddon and R. Church. (1955) *Brit. med. J.*, ii, 1360.

Twenty-two cases of pemphigoid are described and the clinical features and differential diagnosis discussed. Of the 11 treated with ACTH, 7 survive, one requiring maintenance therapy. Attention is drawn to the increased risk of death due to thrombophlebitis and embolism with this therapy.

Of 11 cases treated before corticotropin was available only four survived.

B. A. T.

MALIGNANT CHANGES IN ERYTHEMA AB IGNE. G. A. Grant Peterkin. (1955) *Brit. med. J.*, ii, 1599.

A description of four cases in which squamous-cell carcinoma developed on an area of erythema ab igne and one case in which there were pre-malignant changes. Two of the patients had formerly had cancer of other organs and two manifested poikiloderma atrophicans vasculare.

The condition is common in women in this country but rare in the United States, probably attributable to the universality of central heating.

Similar cutaneous changes due to heat from the kangri bowl in Kashmir and the kang bed in China have been shown to produce cancers. B. A. T.

PRURITUS. D. I. Williams. (1956) *Practitioner*, **469**, 176.

Pruritis may be due to external causes that include parasitic infestation, contact with wool and occasionally bath salts or antiseptics. Internal diseases such as visceral cancer, reticulosis, diabetes, jaundice, renal disease and drugs may be responsible. Frequently there is no organic cause, and psychological factors, especially a desire for sympathy and escapism, are important. Occasionally frankly psychotic patients with parasitophobia itch and scratch interminably.

Treatment is directed towards the underlying cause and local applications such as 1% tar or phenol in calamine liniment, Eurax lotion or cream are recommended. Cotton should be worn next to the skin, and internally aspirin, codeine or chlorpromazine are useful.

R. J. C.

ACNE VULGARIS. P. F. Borrie. (1956) *Practitioner*, **475**, 176.

Acne vulgaris results from excessive sebaceous secretion with obstruction of the pilosebaceous orifices. Retention of sebaceous material induces a foreign body type of inflammation and subsequent secondary infection. Increase in the ratio of either androgen or progesterone to oestrogen may be an important aetiological factor.

Treatment should be directed towards relieving the pilosebaceous obstruction by manual removal of blackheads, frequent washing and the local application of sulphur and astringent lotions. In certain cases ultraviolet light, freezing with carbon dioxide snow and radiotherapy may be used. General treatment is also important. R. J. C.

PARASITIC INFECTIONS OF THE SKIN. J. M. Beare. (1956) *Practitioner*, **484**, 176.

An excellent summary of the infestation encountered in the United Kingdom, including human and animal infection with mites, fleas, lice and ticks. R. J. C.

DISEASES OF THE NAILS. B. C. Tate. (1956) *Practitioner*, **497**, 176.

The common diseases of the nails are summarized. R. J. C.

TREATMENT OF ECZEMA IN INFANCY AND EARLY CHILDHOOD. R. P. Warin. (1956) *Practitioner*, **502**, 176.

An excellent summary of the modern views and treatment of this troublesome disorder.

R. J. C.

TINEA PEDIS IN GENERAL PRACTICE. W. Gould and M. Schwartz. (1956) *Practitioner*, **670**, 176.

Forty-five cases of tinea pedis were treated with " Penotrane." Good or very good results were obtained in 80% of the cases. R. J. C.

THE TREATMENT OF IMPETIGO. J. McMaster. (1956) *Practitioner*, **673**, 176.

Fifty-seven cases of impetigo were treated with "Graneodin" (neomycin and gramicidin) ointment. Complete clearance of the infection was observed within three to seven days and there was no evidence of sensitization to the ointment. R. J. C.

DRUG ERUPTIONS. E. J. Moynahan. (1956) *Practitioner*, **510**, 176.

A drug eruption may mimic almost any skin disease. It is usually produced by hypersensitivity reactions, but other mechanisms include enzyme inhibition. Certain chemical groupings are particularly allergenic such as those with a benzene ring as a nucleus and to which a labile $-NH_2$ or chlorine atom is attached. The pyrimidine nucleus is also antigenic. The history and appearance of the eruption are more helpful in reaching a diagnosis than skin tests. The commoner drug rashes are described. R. J. C.

COSMETICS AND THE SKIN. G. Hodgson. (1956) *Practitioner*, **520**, 176.

A useful summary of eruptions due to lipstick, eye "make-up," nail preparations, hair preparations, face creams and powders, perfumes, deodorants, etc. R. J. C.

INSECT BITES AND STINGS. J. M. Beare. (1956) *Practitioner*, **690**, 176.

Black-flies (Simulidae) are found in Britain and the bite may be more painful than a mosquito bite, causing a hard swelling. Biting midges (Ceratopogonidae) are a major pest in Scotland. The effect of the bite varies in different victims as well as with different species of midge. An immediate urticarial or delayed papular type of reaction may follow mosquito bites, whereas horseflies (Tabanidae) may produce a large blister with considerable oedema and lymphadenitis. The best local treatment is liberal application of calamine lotion. Dimethyl phthalate is an effective repellant. The stings of ants, bees, wasps and hornets are more dangerous and may cause an anaphylactic shock. R. J. C.

EXPERIMENTAL STUDIES ON THE EFFECT OF HORMONES ON THE HUMAN SKIN WITH REFERENCE TO THE AXILLARY APOKRINE SWEAT GLAND. W. B. Shelley and M. M. Cahn. (1955) *J. invest. Derm.*, **25**, 127.

A total of 170 "deep surgical excision" biopsies, with an average of 300 serial sections of each of them, were undertaken in order to exclude any effect upon the aporine glands of oestradiol, testosterone, progesterone, pituitary growth and gonadotropic hormones, chorionic gonadotropin and prolactin applied locally or ingested, alone or in various combinations. All subjects receiving progesterone reported generalized eccrine hyperidrosis, a symptom stated to be common in pregnancy and at the menopause. J. H. T. D.

HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. VIII MITOCHRONDRIA IN THE SEBACEOUS GLANDS. W. Montagna. (1955) *J. invest. Derm.*, **25**, 117.

Mitochondria in the cytoplasm of sebaceous glands—even in the covering epithelium—can be stained with Regaud's haematoxylin or Altmann's aniline acid fuchsin with methyl green provided that the slices of tissue are no more than 1 mm. thick and have been well cooked in 3% potassium dichromate.

The author's findings suggest that while their debris may constitute part of the phospholipoid component of the secretion the mitochondria are not directly converted into plain lipoid. J. H. T. D.

EXPERIMENTAL STUDIES IN DRUG-RESISTANCE OF DERMATOPHYTES. I. THE DEVELOPMENT OF DRUG RESISTANCE OF TRICHOPHYTON MENTAGROPHYTES AND MICROSPORON LANOSUM TO UNDECYLENIC ACID AND 2-DIMETHYLAMINO-6-(B-DI-ETHYLAMINOETHOXY) BENZOTHIAZOLE DIHYDROCHLORIDE (ASTEROL). E. Grunberg and E. Titsworth. (1955) *J. invest. Derm.*, **25**, 113.

The attempt to foster the development of resistance consisted in seeding the plate having the next higher concentration of the fungicide with colonies producing normal growth in the plate below.

In the case of undecylenic acid it was found possible to raise the tolerance from 0·01% to 0·04% for both organisms; in that of Asterol 16- to 32-fold but still within the range in which an atypical growth had always been possible. J. H. T. D.

THE EFFECTS OF DRUGS ON THE PROTEIN-BOUND — SH AND S-S GROUPS OF HUMAN SERUM. R. W. Goldblum and W. N. Piper. (1955) *J. invest. Derm.*, 25, 139.

Exposure of serum to U.V.R. either multiplies or activates the — SH and S-S groups in it. Provided that they are added to the serum before the exposure, coupling takes place in varying degree with sulphanilamide, P.A.B.A., gantrisin, atebrine and 8-methoxypsoralen, but not if they are added afterwards. It is less likely that the drugs inhibit, by their light-absorbing properties or otherwise, the activation of the — SH groups. J. H. T. D.

COMPARATIVE STUDIES OF ENTERIC BACTERIAL FLORA IN ACNE VULGARIS. D. E. Loveman, R. O. Noojin and C. H. Winkler. (1955) *J. invest. Derm.*, 25, 135.

Material obtained by swabbing the empty rectum was directly streaked on plates of blood agar with and without sodium azide, of MacConkey and of *Salmonella-Shigella*, and the swab was finally dipped into thioglycocollate broth.

Streptococci, bacteroides, *E. coli*, *Str. faecalis*, *pseudonomas*, *diphtheroids*, *Staph. aureus*, *Staph. albus*, anaerobic staphylococcus, *Clostridium Welchii* were found more or less uniformly not only in patients of both sexes between 12 and 20 with pustular acne but also in normal males aged between 21 and 30. J. H. T. D.

THE EFFECT OF SALICYLAZOSULPHAPYRIDINE (AZULFIDINE) ON PUSTULAR ACNE VULGARIS AND CERTAIN OTHER DERMATOSES. E. P. Schoch and C. H. McCutchion. (1955) *J. invest. Derm.*, 25, 123.

"There is no question that salicylazosulphapyridine is a *definite adjunct* in the control of the pustular phase of acne vulgaris and of several other dermatoses which have an *infectious element*. It does not however seem to influence the underlying *pathologic defect*."

J. H. T. D.

THE *IN VITRO* SENSITIVITY TO ANTIBIOTICS OF ORGANISMS FOUND IN ASSOCIATION WITH SOME CUTANEOUS DISORDERS. W. Lewin and L. J. A. Loewenthal. (1955) *J. invest. Derm.*, 25, 157.

The idea is that if for some skin disease thought to be produced by pus cocci you prescribe an antibiotic at random or merely on the recommendation that it has a broad spectrum you stand at least a 70% chance of failure, whereas presumably—and indeed according to a paper published in a journal devoted to the subject of antibiotics quite certainly—you stand a better chance if you select your antibiotics on the strength of *in vitro* tests.

On the other hand the authors are ready to accept evidence that prolonged use of an antibiotic —selected at random, whether or not prescribed in dosage that could be expected to exert a suppressive effort, and even where it is granted that the antibiotic is active against only a few of the microbes involved—is often successful. The possibility of indirect effect through some influence on the intestinal flora is discussed; but that patients who are cured (i.e. treated devotedly) often get well in spite of it has been overlooked. J. H. T. D.

RESPONSES OF THE SUPERFICIAL PORTION OF THE HUMAN PILOSEBACEOUS APPARATUS TO CONTROLLED INJURY. A. Z. Eisen, J. B. Holyoke and W. C. Lobitz. (1955) *J. invest. Derm.*, 25, 145.

If the epidermis including the infundibulum of the pilosebaceous follicle is mechanically destroyed, regeneration of the covering epithelium can start from cells of the external root sheath and of the duct of the sebaceous gland. That such cells may retain part of their capacity to engender sebaceous gland is shown by the occurrence of nests of abortive gland tissue in the covering epithelium. J. H. T. D.

THE DISTRIBUTION OF RADIOACTIVE IODINE (I-131) IN EXPERIMENTAL COCCIDIOIDOMYCOSIS AND SPOROTRICHOSIS. T. H. Sternberg, V. D. Newcomen, C. G. Steffen, M. Fields and R. L. Libby. (1955) *J. invest. Derm.*, 24, 397.

We still do not know precisely how iodides influence certain granulomas; but this paper, even if its experimental data leave certain question unanswered and pose yet further ones, does give an excellent idea of what people have been thinking on this subject. Earlier experiments with tuberculosis and syphilis have been held to show a tendency for granulation tissue to concentrate iodine; but I^{131} now makes possible a closer study of its metabolism.

Sporotrichosis is a mild chronic infection in the mouse, coccidioidomycosis a rapidly fatal illness. Both produce granulomatosis of the omentum. Iodine has no therapeutic value in either disease though it is of course effective in the sporotrichosis of man.

The thyroids of mice infected with either disease take up less I^{131} than the normal, possibly because the secretion of thyrotropic hormone may have been suspended in favour of ACTH. Normal liver stores two or three times as much iodine as normal omentum but the granuloma of coccidioidomycotic mice (easier written than said) takes up twice as much as the liver. In sporotrichosis, by contrast, the livers could store two or three times as much as the granulomas which in turn took up very little more iodine than ordinary tissue.

The above is true of tracer dosage. When non-radioactive iodine was added to make the dosage up to substantial therapeutic levels it was no longer possible to discern any altered capacity for concentration or storage. J. H. T. D.

ON THE VIRUS AETIOLOGY OF PEMPHIGUS AND DERMATITIS HERPETIFORMIS. A. Marchionini and Th. Naseman. (1955) *J. invest. Derm.*, **24**, 267.

A survey of the literature, followed by an account of an investigation, of 11 personal cases of pemphigus 4 of D.H. and 1 of p. vegetans. Staining for elementary bodies, electron microscopy, chorion-allantoic culture and intra-peritoneal -cerebral and -corneal inoculation, were employed. J. H. T. D.

RESULTS OF SURGICAL TREATMENT OF INTRACTABLE CASES OF LEUCODERMA (VITILIGO) IN A SERIES OF 58 CONSECUTIVELY TREATED CASES. Vasant P. Mehta. (1956) *Antiseptic*, **53**, 175.

Excellent results are reported from lightly abrading the surface of patches of vitiligo with an electric drill and then tattooing the area with an oscillating needle (120/min.). A " melanin-like " powder is compounded to the exact shade required and used in the form of a paste. No details are given. There were no complications. R. D. S.

EXTRACELLULAR CHOLESTEROLOSIS. R. V. Rajam, V. C. Anguli and A. S. Thambiah. (1956) *Ind. J. Derm. Vener.*, **22**, 1.

Two cases have been previously published under this title by Urbach and Laymon in 1932 and 1937 respectively. The authors describe a third, a male aged 25 with a three years' history of numerous yellowish or brown tumours on his palms and soles, by the knuckles, and in the vicinity of the elbows and knees. Clinically the similarity to xanthoma tuberosum was close. No systemic involvement was found and no abnormality in the blood. Histologically there was a dense infiltrate containg no foam cells or Touton giant cells, but apparently many histiocytes and there was much vascular proliferation, the endothelium often being degenerate. Around the periphery there was considerable formation of new collagen, disposed in whorls. Throughout the whole lesion droplets of fat lay free in tissue spaces, and tended to be arranged particularly around blood vessels. R. D. S.

THE OSLO STUDY OF UNTREATED SYPHILIS. REVIEW AND COMMENTARY. L. W. Harrison. (1956) *Brit. J. vener. Dis.*, **32**, 70.

To be appreciated this paper should be read in full and it will be to the advantage of all practising venereologists to do so. W. G. A.

SOME OBSERVATIONS ON THE TPI TEST. ASSESSMENT OF RESULTS ACCORDING TO CLINICAL DATA. INFLUENCE OF SOME VARIABLES ON PARTIAL SPECIFIC IMMOBILIZATION. N. Hardy, L. J. Borel, G. Daguet and P. Durel. (1956) *Brit. J. vener. Dis.*, **32**, 91.

The TPI test used diagnostically gives frankly positive or negative results. Variables in practice offset one another, and they do not affect the reproducibility of the qualitative test which has proved to be very satisfactory. W. G. A.

AN EXAMINATION OF KAHN'S UNIVERSAL SEROLOGICAL REACTION AS AN AID TO THE DIAGNOSIS OF SUSPECTED LATENT SYPHILIS. A. E. Wilkinson. (1956) *Brit. J. vener. Dis.*, **32**, 98.

Differences were found in precipitation patterns between sera from patients with syphilis and sera from patients thought to have given non-specific reactions, but these differences were not

sufficiently constant to allow undue reliance to be placed on the Universal Reaction as means of distinguishing such non-specific reactions. W. G. A.

CUTIS MARMORATA TELANGIECTASICA CONGENITA. L. E. Pierini and D. Grinspan. (1955) *Arch. argent. Derm.*, **5**, 295.

A description of two male patients with no family history of the condition. In addition to the usual lesions both had indolent ulcers on the heels, and one had lesions on the mucous membranes in addition to palms, soles and scalp. G. W. B.

A CASE OF LIPOIDOPROTEINOSIS. J. M. Borda and J. Abulafia. (1955) *Arch. argent. Derm.*, **5**, 311.

They describe a typical example. There was no family history of this affection but the parents were related (uncle-niece) and the grandfather-uncle was diabetic. G. W. B.

MYCOSIS FUNGOIDES AND VITAMIN B_{12}. N. Gollnick. (1956) *Actas dermo-sif., Madrid*, **47**, 380.

Two patients suffering from mycosis fungoides were treated with large doses of vitamin B_{12} 1000 μg. injected on alternate days. Subjective symptoms improved rapidly in twenty-four hours. After the lesions had subsided a maintenance dose of 30 μg. daily seemed to keep the patients under control. Gollnick says that the temporary improvement is comparable with that achieved by x-ray therapy. He draws attention to Hesse's report on similar improvement when taking two litres of whole milk daily and to the very high content of vitamin B_{12} in cow's milk. G. W. B.

LIPOID STORAGE DISEASES AND NON-LIPOID HISTIOCYTOSIS. R. B. Scott. (1956) *Practitioner*, **148**, 177.

The adult type of Gaucher's disease commonly shows characteristic pigmentation, resembling chloasma uterinum on the face, with a grey or brown pigmentation of the legs extending from the instep to the knee. In essential hypercholesterolaemic xanthomatosis a common finding is xanthelasma palpebrarum. Less often, nodular xanthomas occur on the extensor surfaces of the arms, the elbows and the buttocks. Xanthoma planum is sometimes seen, most often on the knees. Fever and a haemorrhagic skin infiltration occur in Letterer-Siwe disease. R. J. C.

SARCOIDOSIS. H. J. Anderson. (1956) *Practitioner*, **160**, 177.

Sarcoidosis can be produced by the tissues of a susceptible human body in response to a great variety of different stimuli, such as tubercle bacilli, beryllium particles and foreign bodies. The histology is characteristic and lesions may be widespread. An unequivocal diagnosis rests upon finding characteristic lesions on histological examination. It may be discovered by chest x-ray as bilateral hilar gland enlargement, fine miliary mottling throughout both lung fields, a fine or coarse infiltration, widespread fibrosis with cystic changes, or one or more large masses in the lung fields. About a third of all cases present as erythema nodosum and about forty per cent of patients have eye involvement. Twenty-five per cent of cases have skin lesions ; either nodules, cutaneous or subcutaneous masses or plaques. The cutaneous lesions may arise at sites of recent trauma with entry of foreign material into the skin, a former inoculation or surgical incision. R. J. C.

NICKEL DERMATITIS. H. T. H. Wilson. (1956) *Practitioner*, **303**, 177.

Eighty-five cases are described of acute sensitivity in women with dermatitis, following contact with nickel-containing objects. In about half the cases an eczema or neurodermatitis occurred elsewhere on the body, particularly the elbow flexures, the eyelids and the sides of the neck. Once acquired, nickel sensitivity appears to persist. R. J. C.

MODERN TREATMENT OF CUTANEOUS TUBERCULOSIS. Cavalieri, R. (1955) *Cronache Dell'Idi*, **9**, 192.

A well-balanced article, setting forward the various forms of treatment and the Italian experience of these. The author concurs with others in accepting calciferol as the drug of choice in lupus vulgaris and iso-nicotinic acid hydrazide in colliquative and ulcerative tuberculosis where bacilli are more abundant. The latter drug is also more effective in papulo-necrotic tuberculides and erythema induratum. Streptomycin and P.A.S. hold an intermediate place. D. S. W.

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